CHARLES ÉDOUARD BRO

A Nineteenth Century N
and Endocrinolo

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Charles-Édouard Brown-Séquard

A Nineteenth Century Neurologist and Endocrinologist

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MAURITIAN STUDENT AND FREELANCE INVESTIGATOR IN PARIS

I

HAD Charles Édouard Brown Séquard been born a half century earlier, it might have been thought that the circumstances of his birth had provided the germ of the plot for *Paul and Virginia*, the romantic idyll which distilled so many pleasurable tears from the eyes of its nineteenth century readers. The author of this tale, Bernardin de Saint-Pierre, just before our own American Revolution, had spent three years in the beautiful but tempestuous little island known at that time as the Isle de France and situated some 550 miles east of Madagascar on the trade route to India. An ardent disciple of Jean-Jacques Rousseau, he published on his return to Paris a series of volumes entitled *Studies of Nature*, in the fourth of which, written in 1789, we find the famous story. It begins with an account of a French lady whose husband left her at Port Louis in the

Isle de France to embark upon a business venture, but died before he could return, his child was born posthumously, the mother endured many trials because of straightened circumstances and made an alliance with another woman in a like situation This is the very story of Brown-Séquard's mother, Charlotte Séquard

Although she herself was born in the Isle de France, she was of pure French descent, for her father, Sieur Pierre-Paul Séquard, had come from Marseilles, and had married in 1787 a French woman from the neighboring Isle de Bourbon, Marie-Jeanne-Elizabeth-Geneviève Nativel Sieur Séquard was engaged in commerce and later became secretary to the triumvirate in charge of the government of the island Three daughters were born, the second, Charlotte, in 1788, and she alone survived infancy, and was brought up by her father, since the mother died when this child was four

In 1810 the British successfully laid siege to the Isle de France and captured it Ever since the French Revolution the island had been a thorn in the flesh of the British, since hardy corsairs used it as a convenient base from which to prey upon British shipping plying to and fro from India Three years later,

on July 28 1813, Charlotte Séquard married a captain in the American merchant marine,[3] Charles Edward Brown, who had been born in Philadelphia of Irish parentage (it is even remembered that the county of origin was Galway) and who was four years older than his bride. In the following year the treaty of Paris confirmed British possession of the Isle de France and its name was now changed back to the original Dutch form, Mauritius. The inhabitants were to be permitted to retain their own laws, customs, religion and speech although they were now British subjects. Mauritius therefore remained essentially French just as the elegance of French taste continued to be reflected in the baroque buildings of the little green and white capital of Port Louis.

Charlotte Séquard and Captain Brown had been married some three years when the colony was again menaced with starvation as it had been earlier during the British blockade. There was a dearth of rice and Captain Brown sailed to India for relief. The ship took on its cargo but never returned to Mauritius. Whether it was lost in one of the violent storms usual in that part of the world or whether it was taken by the pirates infesting the Gulf of Bengal was never known for certain.

On April 8, 1817, at eleven in the morning, Charles-Édouard Brown was born, a posthumous child and a British subject, and he was named for his father His birth certificate bears as chief witness the name of his maternal grandfather, who was then aged sixty-four Captain Brown left no estate and his widow was thrown upon her own resources The story goes that she was greatly supported by her friendship with Madame Chauvin, a neighbor with young children of her own, who even acted as wet nurse when the maternal supply failed temporarily for the infant Brown As time went on Charlotte Brown undertook to earn a living for herself and her son by her needle According to one report, she had a small dress-making shop, according to another, there was an aged negress, bearing a marked resemblance in her devotion to the faithful slave in *Paul and Virginia,* who sold her embroideries for her The grandfather helped by keeping an infant school Young Édouard, for, judging from his signature in later years, he must have been called by his second Christian name, was probably first taught by his grandfather His more formal elementary schooling was obtained at the Pensionnat Singery, where Jules

Chauvin the son of his mother's friend and a good friend of his own was also in attendance

When he was about fifteen the boy felt the need to help out the family fortunes and he left school to act as clerk in the great general store of Port Louis It is said that this establishment was like an oriental bazaar It sold everything from vegetables to books, and it was the substitute for a *café* in Paris as a meetingplace for amateur poets and dramatists and other artistic souls As young Brown went about his regular duties he had the opportunity to hear authors declaim their own works and he also had access to books on the shelves of the store He was moved to try his own hand and the resulting tales, plays and verses were well received by the local critics

The immediate purpose served by this literary activity was in helping the young man's friends to recognize his great intellectual promise, and by the time he was twenty they were agreed that Paris was the only place to develop his unusual talent Some of them, under the leadership of his childhood friend, Jules Chauvin, clubbed together to send him to France to complete his interrupted education His mother chose to share his adventures and the two

left Mauritius together on January 8, 1838, on a sailing vessel bound for Nantes The voyage became a legendary one in the family We have the testimony of the third, and yet unborn, generation that it took eleven months, since it was before the time of the Suez Canal and the ship was becalmed for two months at the equator However, the Browns did reach harbor in Nantes, and eventually Paris, before the end of 1838, for Charles-Édouard passed his baccalauréat in Letters in November of that year as a necessary preliminary to his enrollment in the École de Médecine

He seems also to have made immediate use of a literary introduction to Charles Nodier (1790-1844), the academician, perhaps in the naive hope that he might be able to maintain himself by means of his pen Here the parallel with the better-known story of Claude Bernard (1813-1878) becomes so close as to awaken scepticism in the historian [2] Bernard, aged twenty-one, fresh from a provincial city and full of hope, had gone to Paris in 1834 to present his literary work to the famous critic, St-Marc Girardin, only to be dissuaded from the pursuit of a literary career and advised to study medicine, advice which he immediately followed Charles-Édouard Brown,

twenty one years old, fresh from a small colonial city and full of hope arrived in Paris just four years after Bernard, he took the best of his literary compositions to Nodier on the recommendation of a compatriot who had already entered literary circles in Paris, but the young Brown, too, was discouraged by his mentor, who rendered judgment in the words, "One must adopt a profession in order to live, my friend" One wonders whether this was a routine procedure with literary critics of the last century, and also how many French physicians owe their final choice of a profession to early leanings toward literature The advice given seems to have been proper in these two cases, at any rate

A letter written about fourteen years later than this by Brown himself to Miss Ellen Fletcher, who later became his wife, makes the influence of Nodier seem less important Brown wrote that he arrived in Paris with a quantity of "plays, poems, pieces of light verse and philosophical bits" in his trunk, he meant to study medicine but hoped "after a while to turn to literature" "But I needed to think of my mother," he added, and so he made a bonfire of all his manuscripts, with the consequence that we are denied, or spared, what would have been a bio-

grapher's inevitable task, a comparison of Claude Bernard's *Arthur de Bretagne* with a drama by Charles-Édouard Brown The latter, after his literary burnt sacrifice, went to work at once to repair the omissions in his early education which prevented his immediate entrance upon his medical studies He prepared for and passed two baccalauréats (in Letters in November, 1838, and in Science in 1839) and he was enrolled in medical school at the end of 1838

The problem of livelihood was solved when Mme Brown rented an apartment in a quiet little street, the rue Ferou, lying between Saint-Sulpice and the Luxembourg Gardens, and established a boarding-house for Mauritian students Édouard laid out for himself a thoroughly Spartan régime in his studies He began a habit which he retained for the rest of his life of going to bed at 8 p m and rising at 2 or 3 a m in order to take advantage of the quiet morning hours for serious work From very early in his studies he had recourse to a device which seems to have been almost customary with the more gifted of French medical students, since it was adopted by Bichat (1771-1802), Dupuytren (1777-1835) and Magendie (1783-1855) of the previous generation

Partly to add to his slender means and partly to fix newly acquired knowledge in his own mind, he organized tutorial classes for his fellow students in the subjects of the first year medical courses in the Faculty of Science, physics, chemistry and natural history. He also enrolled as a pupil at the laboratory of Dr Martin Magron (1810-1872). It was the custom at that time for those interested in physiological research to set up private laboratories and take pupils to defray expenses. From all accounts, few of these enterprises proved sources of much financial profit. He was maintained for a time by Claude Bernard hardly paid for the animals used. In his second year of medical study Brown became aware of a special interest in physiology and turned his connection with the Martin Magron laboratory to account by using it as a convenient place in which to repeat experiments which were described or performed in the medical course, or even to try out original ideas of his own. His relations with Dr Martin Magron would seem to have been mutually pleasant and profitable, for the association was continued for several years, and joint papers were eventually published.

A letter written by his mother to a friend in

Mauritius reveals the narrow rhythm of these early student days

I am happy to see the behaviour of my son, so young and yet able to impose upon himself so many hardships He has been to the theatre only once He knows nothing of the pleasures of Paris, never goes out unless his work calls him He leaves me every day in the daytime to take a lesson in chemistry, and goes from there to the hospital to learn to dissect He is determined to learn this and works at it with pleasure and passion, he would like to know everything and understand everything at once

His own feelings about the rebuff to his literary ambitions and the change in his interests was expressed to a friend in another letter

If sometimes my heart still bleeds, my mind at least no longer offers resistance, I have no more dreams of literary glory, no more unbridled longings to make a name in literature, dreams and longings which have followed me for a long time I have rid myself of all that, and now I aspire to nothing more than my diploma in medicine

In July, 1839, halfway through his first year, he wrote

I have so much to do that I have to live like a savage, like a bear I want to know something more than the

general run of doctors in Mauritius I shall try for a place as *externe* in the hospitals at the end of next year

By 1840 he had begun to feel as if he had left his youth behind him He wrote

> The necessity I am in to create for myself in Paris such a position that I may be able to live in comfort with my mother entirely on the product of my own efforts, this necessity has matured me early, entirely metamorphizing me from a child into a man, has unhappily made me perhaps a little dull

He probably felt that a young man who gave lectures in " physics, chemistry, natural history and (by 1842) physiology " was bound to appear a little sober to his listeners, who were of the same age as their instructor

In 1842 he and Charles Robin (1821-1885) were both *externes* together on the service of the famous clinician Trousseau (1801-1867) They lived near each other not far from the medical school and used to meet in the morning on their way to the hospital They studied together for the competitive examination for an interneship, and, according to the recollection of Brown many years afterwards,[8] although Robin worked even harder than he did, Robin got a lower grade because he had difficulty in expressing

himself The apprenticeship served to literature in Mauritius was not utterly wasted after all

At the moment when at last all seemed to be going well, young Brown got an infection from pricking his finger in the dissecting room The accident came close to costing his life and for some months during 1842 he remained very ill He was scarely recovered when his mother suddenly died This was a staggering blow He was of an affectionate disposition and the circumstances of her widowhood had made his mother especially close to him The natural tie between them had been forged doubly strong The impulse to escape from the desolation of Paris overcame him, and this first flight set a pattern which he was always to follow Whenever a situation became too much for him, he promptly set off on an ocean voyage On this occasion, he set sail from Le Havre, December 13, 1842, on the ship *Bougainville* bound for Mauritius, and he arrived at Port Louis March 24, 1843 At once he saw his mistake He could never be content to remain on the small island of his birth He must return to Paris and his medical studies at once

It took a little time to arrange matters, for in June, 1843, he was still in Mauritius according to the testi-

mony of the records of the local Society of Natural History. He had been unanimously elected to membership in this society at its preceding meeting and on the first of June he presented a paper on a waterspout which he had seen in February while still at sea. However the scientific resources of Mauritius did not detain him for long. He appealed to a friend to pay his passage back to France, and before the end of the year he had resumed his interrupted medical studies in Paris.

It is a little uncertain from records immediately available whether Brown served the internship for which he had qualified along with Robin before his illness in 1842. The modern arrangement is that when a student accepts the four year appointment as *interne* for which a successful candidacy at the competitive examination has made him eligible, he cannot graduate until he has completed the service. Only a little over two years elapsed between Brown's return to Paris at the end of 1843 and the presentation of his thesis January 3, 1846.[4] There is evidence of his being engaged in activities outside the hospital routine, for he carried on a series of experiments in Dr. Martin-Magron's laboratory which resulted in his name appearing for the first time in the *Comptes*

rendus of the Paris Academy of Sciences This brief mention occurred in November of 1844 when he and Martin-Magron together deposited a *paquet cacheté* to secure priority for some of their work These sealed packets, more often than not, were never referred to again, but if a rival scientist did come out with a paper embodying the idea expressed in the sealed deposit, the author could demand that it be opened and thus establish his priority

A problem in which Brown was interested at this time concerned gastric juice Evidently he had been reading the account of Réaumur's famous buzzard, for he swallowed sponges to absorb his own gastric juice and then drew them out to recover their contents, much as Réaumur (1683-1757) had done on his birds a century before This rather uncomfortable experimental procedure led to persistent rumination, technically known as *merycism*, a condition in which once swallowed food returns to the mouth for further mastication Brown reported later that for years after this series of experiments he felt unsafe in polite society during a meal and was nervous about accepting invitations to dine

Also carried out in the Martin-Magron laboratory was a series of experiments on the nervous system,

the results of which were to serve as his thesis for the degree of M D , and the thesis was written under the doctor's guidance It was dedicated "À ma mère," and signed "C E Brown" The summary of its contents made fifteen years later under the direction of its author ' was as follows

This work is composed of two distinct parts the first has for its object the study of reflex movements in batrachians, especially the augmentation of the reflex faculty after section of the cord, ° the second treats of the properties and functions of the columns of the cord and has for its chief aim the demonstration that the transmission of sensation is by way of the gray substance and not by the dorsal (posterior) columns In this second part the author remarks that pricking the anterior columns of the cord in frogs, eels, pigeons, rabbits and dogs, causes only local contractions, an important fact which shows the *inexcitability* (the italics are Brown's) of the longitudinal fibers of the anterior columns

In the introduction to the thesis Brown mentions that he had done the experiments for the first part with Dr Martin-Magron, and at the same time he makes handsome acknowledgment of his gratitude to his friend and teacher "for the liberality with which the treasures of his heart and mind had been laid open" to his pupils The experiments for the

second part would seem by implication to have been done independently, and this is of interest because it is in the second part that we find the germ of the discovery which was eventually to be established as his major scientific achievement

The prevailing doctrine that sensations were conveyed in the cord by its dorsal (posterior) columns to the cerebrum, the " common sensorium," had been sponsored with fierce partisanship by Sir Charles Bell (1774-1842) in England and by F H Longet (1811-1871) in France Not long after Brown began his medical studies, Longet had published his researches on the functions of the different columns of the cord and of the spinal nerve roots, prefacing his own work with an " historical and critical examination of experiments made on these structures since Sir Charles Bell " [7] Longet was essentially in agreement with Bell, since he concluded that the latter's doctrine was " one of the most beautiful, the most fecund and withal the *best established*, as we claim to have shown elsewhere, even to the most critical of minds " The sensory aspects of Bell's doctrine, considered by Longet from the experimental point of view, could be stated thus stimulation of the dorsal columns, particularly in the cephalic

regions, gives very evident signs that sensations of pain are perceived, stimulation of the ventral and lateral columns, or of the gray matter gives no evidence of pain Brown's thesis was a protest against these statements He, too, had examined the question from an experimental point of view, but one which was complementary to that of Longet He emphasized the effect of extirpation of parts, although he also investigated the effect of stimulation He performed the delicate operation of sectioning either the posterior columns of the spinal cord in cold-blooded animals, birds and mammals, or the antero-lateral columns, or both together He found that sectioning the antero-lateral columns led to complete paralysis of voluntary movement, but there was no interference with sensation If the posterior columns were sectioned, there was some loss of voluntary movement in the warm-blooded animals (not in the cold-blooded), but again " sensations persisted without great diminution in the parts situated behind the sections " [8] The results of sectioning both columns was diminution of voluntary movement, but he stated, " I have found the parts situated behind the section and on the same side to be seemingly as sensitive as those on the sound side " This, as stated,

is rather disturbing, since if the operation had been properly performed there should have been some diminution of sensation on what he termed "the sound side" posterior to the section, although in an animal this would not be easily determined since purely spinal reflexes would, of course, be present These experiments, therefore, did not demonstrate actual crossing of sensory fibers in the cord, the point of the completed discovery, but were nevertheless most suggestive That the idea was in his mind is shown in the last paragraph but one of the thesis "I should point out another important fact, shown by my experiments, the facility with which sensory impressions are transmitted from one side of the cord to the other"[9] The heresy implied in these descriptions of Brown's experiments passed unnoticed in a mere doctoral thesis The first stone from David's sling had bounced without effect off the head of the Goliath sponsored by Bell and Longet, and some three years had to elapse before more formidable ammunition was available to the assailant

2

Immediately after obtaining his medical degree, Charles Édouard Brown entered upon a most trying period in his personal and professional life He was desperately poor, and yet he seemed to have forgotten completely the intention, proclaimed in his letter of 1840, of making the practice of medicine the means to a comfortable life He was fully determined to continue the investigations so promisingly begun in Dr Martin-Magron's laboratory, the first fruits of which had been harvested for his doctoral thesis Even his experimental material was a charge upon his slender resources, and the legend is that most of the time he had nothing to eat but dry bread and plain water, while living in a wretched unheated room of which the tenancy was shared by the rabbits and the guinea pigs Certainly, his landlady, in allowing him the freedom of his bedroom in this way, must have been more indulgent than the stony-hearted gorgons who presided over the impecunious students of one's own generation in the lodging houses of the Latin Quarter In a letter written many years later regarding the disposition of

some surplus laboratory animals, he gave directions to have the tortoises and guinea pigs killed and the rabbits *eaten*

It is in the signatures appended to his earliest scientific communications after taking his medical degree that we observe the addition of his mother's name to his patronymic, in order, as he said, "to distinguish myself from all the other Browns" The double name first appeared in the *Comptes rendus* of the Academy of Sciences in October, 1846, as Brown-Léquard,[10] later as Brown-Lequard, Brown-Seguard and Brown-Séquart, before the secretary finally grasped the correct combination For the rest of his life he was known as Brown-Séquard, although for a time on official documents he was still Brown, until the new usage was regularized twelve years later by application to the British consul resident in Paris

A helping hand in his continuing practical difficulties was extended early by Dr Charles Rayer (1793-1867), who was a good friend to several of the struggling scientists of this period, and to whose hospital service the young Brown had been attached toward the end of his medical course Rayer sent to the younger man in his character of physician certain

patients who in Rayer's opinion, would be benefited by application of the galvanic current, the new treatment for nervous ailments made popular by Magendie's enthusiastic use of it. This in its modest way was probably the beginning of Brown Séquard's future practice as a neurologist. Du Bois-Reymond (1818-1896) had just invented his induction coil and described the technique of faradic stimulation. With the publication in 1848 of the first volume of his *Animal Electricity* all physiological laboratories began to use this new method of stimulation. The old term "galvanize" which meant stimulation by means of the direct current from an electric cell or battery, remained in use, and it is often difficult to know in reports of experiments about that time whether the direct (galvanic) current was employed in a given experiment or the rapidly repeated induced (faradic) current. Brown-Séquard almost invariably used the older term, although we know that Rayer in 1849 lent him one of the new induction machines, so that from that time on he employed faradic stimulation both in his medical practice and in his experiments.

Another aspect of Brown-Séquard's early medical practice was his attendance, beginning in 1848, at the

military hospital Gros-Caillou, where a year later he distinguished himself by his devotion to duty during the cholera epidemic of 1849 as auxiliary physician under Baron Larrey

Although all his energies were absorbed by this emergency while it lasted, in more normal circumstances his activities were focused on his physiological investigations, and to a free-lance scientist, eager for association with other physiologists, the founding of the *Société de Biologie* in May of 1848 was a circumstance of fundamental importance The chief feature of the meetings was to be free discussion of every communication presented before it It was Rayer's pet scheme and he was made permanent president Claude Bernard, who was always to appear as Brown-Séquard's rather more successful rival in physiology, and Charles Robin, who was already making a name for himself as a histologist, were to act as vice-presidents Meetings were to be held at 3 p m on Saturdays in Robin's amphitheatre at *l'École pratique* At first, two secretaries were chosen, but within a few months there appeared to be need for two more and Brown-Séquard was chosen to be one of them As in the case of the Academy of Sciences, his name appears in the early

records of the *Société de Biologie* spelled with a "t" instead of a "d" This society was always his favorite He much preferred it to the more formal and internationally known Academy of Sciences, and he was apt to refer to it briefly and affectionately as "the Biology"

The index of speakers and topics at the sessions of the new society during its first year, 1849, makes it appear almost as if Brown Séquard had kept up a running monologue with occasional interruptions by Claude Bernard and still rarer ones by Robin and by Rayer, the president Brown Séquard has 35 titles, Bernard 21, Robin 13, and Rayer 15 With very few exceptions other names appear only three or four times Brown Séquard s communications seldom occupy more than two pages and many of them are single paragraphs, so that although the list is lengthy and the topics show very great activity on the part of the experimenter, the actual output of scientific work by Brown-Séquard during these early years is not quite so phenomenal as at first appears At the end of six years of work he had the almost incredible number of an even 100 titles, and before he died the number was over 500, of which a notable proportion

appeared under the auspices of the *Société de Biologie*

He was an acute observer and all the accidental observations which he made in the course of more serious work were meticulously recorded, such as the peculiar disposition of muscles in the caecum of his rabbits, their tumors and their parasitic worms, the coagulability of frog's blood in winter, and even the hibernating habits of the tenrec, a mammal peculiar to Mauritius He included odd items in his own physiology, e g , vigorous sweating on the face when he ate very strongly flavored substances, and he demonstrated this peculiarity before the Society by eating chocolate in their presence The notes read " In less than five minutes his face was bathed in sweat " [11] He reported on the effects of stimulating the human skin by means of the large induction apparatus lent him by Rayer, particularly the somewhat startling results of the application of " electromagnetism " to the human scrotum, but on the occasion of this report he was content to use as his illustrative material before the Society merely the effects on the skin of the arm of a paralytic patient

A rather spectacular instance of his use of the induction apparatus in his practice occurred in 1851,

although he did not report it until many years later [12] He was beginning to gain a reputation for his knowledge of the functions and disfunctions of the nervous system and he was summoned by a police commissioner to examine a young woman of about twenty-one to determine whether her peculiar behaviour was symptomatic of a disturbed mental state or merely feigned Every Sunday morning at the first stroke of the bell in the tower of Saint Sulpice at eight o'clock she would mount on the slippery curved rail of her bed and remain continuously on tip toe, body erect, head thrown back eyes wide open and looking up, saying prayers to the Virgin for twelve long hours until the same bell rang at 8 p m The exhaustion after this effort was so great that the girl was confined to her bed for the remainder of the week, only to rise and assume the same posture the next Sunday morning People thought it a miracle and were beginning to flock to see the spectacle Not long before this Bernadette Subirous had set Lourdes and all France agog with her visions in spite of the combined opposition of Church and State The police commissioner was anxious to prevent Paris being upset by similar religious disturbances Brown-Séquard, accompanied by two pupils, one of whom

was the Mauritian, Bonnefin, and the police commissioner, visited the girl's bedroom one Sunday, bringing the large induction machine from the laboratory While the girl maintained her strained attitude on the slippery bed railing, Brown-Séquard arranged to give her severe electric shocks on the cheek The current caused strong contractions of the facial muscles, but she retained her erect posture unchanged, nor did she cease praying, although the words were enunciated with difficulty because of the forcibly contracted facial muscles The police commissioner remained sceptical until application of the same strength of current to his own cheek made him jump and let out a loud yell of pain The cataleptic state was genuine and Brown-Séquard was impressed at the astounding "nervous force" exerted under the influence of the mind He kept the patient under observation for several months, but when he left Paris he lost track of her The police commissioner succeeded, however, in preventing the spread of publicity and interest in the case soon died out

The topic of "nervous force" was a favorite one He even tried to measure it by the metric system In a discussion under the title "Nervous force in the spinal cord" in February, 1849, he stated "The

spinal cord of frogs separated from the brain, can produce enough nervous force in 24 hours to lift, with one of its hind legs from 100 to 250 kilograms by fractions to a height of 2 to 5 millimetres."[13] Although one would ordinarily think of weight lifting as a property of muscle, nevertheless reflex contraction of skeletal muscle is initiated by a nerve impulse, and the weight lifted by contraction might therefore be considered an indirect measure of nervous action. Brown-Séquard's concentration on the nervous system led him to think of any end result, in this case muscular contraction, in terms of the nervous system.

From the very first there were indications that the meetings of the *Société de Biologie* would always be enlivened by differences of opinion between Brown-Séquard and the other members. In the first month Bernard outlined his ideas on the possibility that loss of motion in certain pathological cases might be due to alteration in the sensory aspects of the spinal cord. He thought that there must be some link between motion and sensation, so that for one of these functions to remain intact the other must be intact also. The report then reads: "M. Brown-Séquart attacks the idea of such an intimate liaison on the grounds of

his own experiments and of pathological cases" After a few further exchanges the report proceeds "On M Brown-Séquart's promising to make a future communication on these questions, the discussion on this subject is discontinued" The value of these discussions is established in subsequent reports which show that the criticism often led to much more precise experimentation than had been described at first

Two days before the end of 1849 Brown-Séquard was elected a member of the *Société philomathique*, in the same section to which Bernard had been admitted nearly three years earlier, and of which Magendie had been a member since 1813 This was one of the societies surviving from the time of the Revolution, having been founded in 1788 Brown-Séquard became its secretary in 1851 He made some reports of his own work before this society, but they were always republished, usually in greater detail, elsewhere

Funds to support his constant experimental activity, no less than recognition, were probably an object when he submitted his work on sensory nerves for the Montyon Prize of the Academy of Sciences As it turned out, he did not win the prize itself, but the

Academy approved Magendie's report that the young man's work was of sufficient merit for him to be awarded honorable mention in 1850, and to be given a sum of money equal to the prize to defray the expenses of his experiments In the same report Magendie announced that Bernard had been awarded the prize for his work on the pancreas With Magendie's loyalty to his most talented pupil to tip the scales, it would seem real generosity on the part of the old professor to recommend equal compensation, although not equal honor, to a rival It was frequently Brown-Séquard's luck to be just a step behind Bernard

Medical students now came to Brown-Séquard to prepare their theses under his direction Two such theses of 1851 are worth mentioning, that of F N Bonnefin, because he was a Mauritian, and because he wrote about the site of action of convulsive poisons, convulsions being one of his mentor's most absorbing topics of investigation, and that of J Benjamin Coste, because it contained an account of experiments, verified by Brown-Séquard himself, on the effects on respiration of transverse cuts made in the brain above and below the medulla These experiments done with Coste were the first of those which led to

Brown-Séquard's scepticism regarding the functions of the respiratory center in the medulla, the " noeud vital," a region whose location had been worked out by Flourens (1794-1867), who considered it essential for the initiation of respiratory movement and for life itself

The rigors of Brown-Séquard's manner of life finally brought about a nervous breakdown, which made itself manifest in disturbances of his digestive system Fortunately for his biographer, he has himself provided, in a rather disguised form, a description of this crisis It is written from the point of view of a physician who in his middle fifties looks back twenty years upon himself as his own patient In 1873, when he wrote the account, he had become bilingual and wrote as fluently in English as he did in French, although the construction of the first sentence is noticeably French

In 1851 I had to treat a very bad case of dyspepsia, and succeeded to cure the patient by a plan of treatment which, I think, deserves attention

The first patient I submitted to this plan was a scientific man, thirty-four years old, of strong constitution, but reduced from several causes to a lamentable state of health For eight years he had been working very hard,

take no exercise and live almost all the time in a vitiated atmosphere. He slept very little and usually passed 18 or 19 hours a day writing, reading or experimenting. His diet was unwholesome and with the object of avoiding the need of much food he took a great deal of coffee. He gradually thereby slowly became exceedingly weak. His digestion which had been very good all his life before he began to work so much had gradually become very bad. He suffered greatly from pyrosis and a feeling of great distress and severe distention after every meal. Acid eructations and vomiting frequently threw up into his mouth and when he did not vomit he found that his food remained in his stomach so long that in the morning he frequently rejected things eaten the previous day. At last he had to give up work and stay in bed. But no improvement occurred from the rest he then had or from various modes of treatment. His constipation and weakness and dyspeptic conditions increased and his friends decided to have him removed to the country. He was so weak that he had to be carried in a litter to the railway station. After a few days feeling that he had not improved, I decided to try a radical change of his alimentation, as regards the quantity of food to be taken at a time. Instead of three meals a day I made him take sixty or more. Every 12 or 15 minutes he took two or three mouthfuls of solid food, chiefly meat and bread. He drank a little less than a wine glass of Bordeaux wine and water every thirty or forty minutes.[14]

The patient, whose identity is not too difficult to guess, improved under this heroic treatment except for the merycism, which persisted to the time of writing Instead of returning to Paris to resume his incessant experimentation, the patient was persuaded to go to the seashore to build up his strength

On the heels of this personal crisis came the Coup d'État of December 2, 1851, and before the next year was out France had once again changed from a republic to an empire Brown-Séquard, like Magendie before him, was an ardent republican, and in the words of E Gley (1857-1903), "arms in hand, he defended the cause of liberty against the Coup d'État" With such a political record against him he thought discretion the better part of valor and decided hastily to leave France

There were other considerations, too Claude Bernard had been fortunate in his long and close association with Magendie Although in 1851 he still held a subordinate position at the *Collège de France*, Magendie as professor was getting along in years and it was a virtual certainty that the assistant would eventually succeed to the chair af Medicine Charles Robin already had a post on the Faculty of Medicine in histology There seemed to be no place for Brown-

Séquard although he was nearly thirty five, had a fine record as an investigator, and had been very successful in giving his private courses in physiology Bernard later, reflecting on his own struggles and those of his slightly younger rival lamented that France did not recognize the talents of her more promising sons and make some effort to foster them, so that these young men might not be obliged to seek their fortunes elsewhere' However in the case of Brown Séquard one must take into account two exceptional factors first although to all intents and purposes he was essentially French, his place of birth made him a British subject, and this fact was an insurmountable obstacle in the way of obtaining one of the coveted positions in the educational hierarchy of Paris, second, the peculiarly restless nature of this scientist of mixed French and Irish blood militated against permanent commitments Some have blamed his inheritance from a sea faring father as being the cause of the periodic flights overseas, of which he was now about to make another The more probable explanation is that having once, at the time of his mother's death given way to the impulse to " escape from it all," the thought of temporary relief through change of scene was strong enough to precipitate

flight Eventually, in addition to one more voyage to Mauritius, he crossed the Atlantic some sixty times, and it has been calculated that he must have spent six years of his life on the sea [16]

For escape this time, instead of returning to Mauritius, he decided upon his father's native land There is evidence that before he left France he tried to prepare the way for a position in the country he was about to enter Since he was to land in Philadelphia, he apparently asked Broca (1824-1880) to write to the authorities of the medical school there regarding his qualifications In February, 1852, Broca wrote to Professor Wood (1797-1879) of the University of Pennsylvania

> For eight years Brown-Séquard has exhausted his resources and imposed upon himself incredible sacrifices in order to carry out expensive researches in experimental physiology Today he has nothing left save an honorable character, profound erudition, and scientific articles which everyone can appreciate

An additional misfortune for one seeking a post in the United States was that as yet he knew no English He therefore chose a slow sailing vessel in which to cross the Atlantic, in order to have time to acquire at

least the rudiments of the language of the country in which he proposed to establish himself

The five years which had passed since the taking of his medical degree had been a period of incessant experimentation, and the break made by his departure for America is a good landmark at which to take stock of his early scientific achievements The eight communications presented in the very first year indicated the direction which much of his future work would take Of these papers of 1847 six were concerned with lesions of the nervous system, one with return of function after perfusion with fresh blood, and one with the iris They told of the following experimental results frogs can exist for a certain time entirely without spinal cords, but they remain alive even longer if the cord is destroyed below the 2nd or 3rd cervical pair of spinal nerves,[17] reflex strength of frogs and birds is not diminished upon severing the brain from the cord, as is shown by the ability of the muscles to lift weights, but is even augmented for a time,[18] the irritability of paralysed leg muscles is temporarily increased after cutting the sciatic nerve,[19] ischemic nerves and muscles recover their irritability upon being perfused with fresh

blood,[20] very dim light, such as that from the moon, can make the pupil constrict[21]

A more extensive survey at once shows that by 1851 he had already accomplished the piece of work which was to make his name significant in the history of physiology He had shown that the nervous pathways for conduction of sensation in the spinal cord cross in the cord, and therefore transverse hemisection of the cord leads to anaesthesia on the opposite side of the body below the lesion and motor paralysis on the same side This condition is still known as the Brown-Séquard syndrome and a knowledge of its mechanism is essential to any diagnosis of injuries to the spinal cord

The beginning of the story has already been told in connection with Brown-Séquard's medical thesis of 1846, in which he presented experimental data in disagreement with the prevailing doctrine, sponsored by Sir Charles Bell and F -A Longet, that sensations were conveyed in the cord by its dorsal (posterior) columns His early experiments, while they failed to demonstrate actual crossing of sensory fibers in the cord, nevertheless suggested that the idea had already taken shape in his mind It would seem from the sequence of the items recorded in the reports

of the *Société de Biologie* for January and February, 1849 that Claude Bernard was partly responsible for Brown Séquard's return to the struggle.[22] Bernard, his attention directed to reflex action, insisted that although modern physiologists agreed that motion and sensation are conveyed by anatomically different pathways in the nervous system, yet 'motor phenomena are intimately linked in their appearance to phenomena of sensation and that in consequence, lesion in sensitive parts, peripheral or central, will lead to lesion or paralysis of movements to an extent proportional to the lesion of the organs of sensation'. Brown Séquard on the contrary, insisted that his experiments showed independence of sensation and motility but he admitted that movements were modified both by cutting the dorsal roots of the spinal nerves and by destruction of parts of the brain, e.g. 'after cutting the dorsal roots, movements of the limbs were awkward less precisely directed, and not so vigorous as before the operation, whereas, after lesions in the anterior parts of the brain, movements were more vigorous and more sustained than normal'.

His next observation was with Dr Tailhé on a case of chronic spinal meningitis where sensation had been preserved, although there had been noticeable

softening of the posterior columns of the spinal cord [23] This observation on a human patient was consistent with Brown-Séquard's experimental findings in rabbits and guinea pigs

He now felt emboldened to attack Longet directly, and was able to show that Longet's criteria for perception of pain, viz, cries and grimaces, were not proof positive that pain had actually been felt, since cries and grimaces could occur reflexly after extirpation of all the cerebrum anterior to the medulla including the *sensorium commune* [24] In other words, he had demonstrated that the common sensorium was not necessarily the destination of all sensory fibers in the spinal cord, as both Bell and Longet thought

In December of this year, 1849, he gave a neat summary of his work to date on transverse section of the spinal cord and here he listed the essential features of the Brown-Séquard syndrome, i e, not only loss of sensation below the lesion on the opposite side of the body and retention of sensation on the same side, but also augmentation of sensation on the same side This is the first clear statement of the famous phenomenon and the author concluded "Even if some sensory impressions are conveyed by

the posterior columns of the cord the majority are conveyed by some other part of this nervous center." In his experiments so far he had made his section in the dorsal segments of the cord and had recorded his observations on the hind leg. Would the same results be obtainable from the fore leg? He soon was able to show that the same conditions did indeed hold for the front leg when the cut was made in the cervical region of the cord.

Once he was sure that most of the sensory path was to cross over in the cord on their way to the brain he thought he now had the secret of the peculiar case of crossed hemiplegia in human patients which were a puzzle to physicians. Influenced by Bell and Longet physicians had considered the nervous lesion in such hemiplegias to be somewhere in the brain itself, on the assumption that a crossing of sensory fibers must take place there, now it was clear that it might be the cord itself which was injured. These results were all presented in a formal paper before the Academy of Sciences in 1850 which may serve as our final reference to the phenomenon at this time.

Although Brown-Sequard hammered away at his point both in the *Société de Biologie* and the Academy

of Sciences, his work was not generally accepted until 1855 when Broca, who already had an established reputation as a neurologist and who ten years later became universally famed for his work on aphasia, read before the *Société de Biologie* his report which finally " overthrew the edifice so securely cemented together, whose foundations had been laid by Charles Bell, and whose capstone had been sealed in place by Longet " [29] This report was nothing more than a recapitulation of Brown-Séquard's work, but with Broca's name to give it weight, the medical world now accepted it, and gave credit where credit was due

These experiments on hemisection of the spinal cord had a curious sequel in that they led to the intensive study of artificially induced epilepsy which occupied Brown-Séquard at intervals for the rest of his life Many of the guinea pigs on the spinal cords of which he operated were kept alive for months, and some of them developed a peculiar epileptiform disease characterized by periodic convulsions These convulsions were so like the disturbances which he had observed in human epileptics that he began a prolonged series of experiments on these phenomena, writing over a hundred scientific articles on the sub-

ject before it died with him—only to be resuscitated, and resolved some forty five years later.

His experiments on *rigor mortis* seem to have captivated his imagination in a manner out of all proportion to their real significance if we may judge from his recurring references to some of the experiments. An early paper on this subject was read before the Academy of Sciences in April 1851.[9] He had found that after the death of his laboratory animals (rabbits guinea pigs and other mammals) *rigor mortis* often set in within a quarter of an hour. If even when the animal's limbs were rigid they were perfused with warm blood, they became sensitive once more and would move not only on direct stimulation of the muscles but on stimulation of motor nerves. About two months later he tried the same procedure on two human cadavers. The account of his experiments on the first is the more dramatic of the two.

Through the good offices of the anatomical laboratory of the Faculty of Medicine he was provided with the decapitated corpse of a healthy young murderer of twenty, freshly guillotined. The execution took place at 8 a.m. The body was allowed to remain untouched, and by 7 p.m. only a few muscles

were sufficiently irritable to respond to strong shocks from the inductorium Even these had lost their irritability by 9 p m , thirteen hours after the execution Brown-Séquard had two of his friends, Dr Bonnefin and Dr Deslauriers, draw half a liter of blood from his own arm They defibrinated the blood in the usual manner by beating and strained out the clots through linen The blood at 19°, a temperature considerably below normal body temperature, was slowly injected into the radial artery in the arm of the cadaver over a period of ten minutes and allowed to flow out of veins which had been opened In about 45 minutes at least twelve separate muscles had once more become irritable He tried further injections of blood the next morning, but by that time the processes of death had gone so far that there was no resumption of irritability Although he made many references later to this experiment, it was always to comment on the possibility of return of irritability after the appearance of *rigor mortis*, and not to suggest an application to the problem of the revival of the organism after "death," in the manner of contemporary Russian physiologists

He did, however, anticipate one of the most

striking of the recent Russian experiments, that of the perfused isolated dog's head. According to Vulpian (1826–1887) who described the experiment in one of his lectures on the nervous system some years later, [1] Brown-Séquard separated a dog's head from its trunk, waited some ten minutes until all traces of excitability were gone, then perfused the head through the vertebral and carotid arteries with defibrinated oxygenated blood. Presently some disordered movements of muscles were observed, then the eyes winked and the facial muscles of expression moved as if the brain were again active and directing the movements. So far as we know, Brown-Séquard did not carry out the suggestion of Vulpian that this experiment be tried on a freshly executed criminal, and that the lips be read to learn what were the criminal's thoughts after death.

A bizarre variant of the perfusion experiments was first tried in 1850 when he succeeded in grafting the tail of a young cat to a cock's comb by stitching the cut edges of the tail to the cut edges of the comb. Some sort of union had taken place in a week, since the cat's tail was warm and bled when pricked, i.e., a continuous perfusion of warm blood had been established through the severed organ. Unfortu-

nately, the cock had a fight with another cock (perhaps the second cock was jealous) on the eleventh day, and in the mêlée the cat's tail was torn off The tissues were still alive and bleeding, which showed that the graft had taken [32]

The best point, which he brought out in a paper of 1849, describing the changes which occur in stimulability and contractility of muscles during the onset and development of rigor, was the rapidity of the appearance and disappearance of rigor if the muscles were maintained in a contracted state after death by means of the electric current This was strikingly demonstrated in a series of animals freshly killed for the purpose At one extreme, an animal in which *rigor mortis* was allowed to develop without interference became rigid at the end of ten hours and remained so for eight days At the other end of the scale, an animal in which most vigorous contraction was maintained by the electric current after death developed rigor in seven minutes and lost it in fifteen It was no wonder that the famous John Hunter (1728-1793) had thought that persons and animals struck by lightning did not develop *rigor mortis*, since the time of its duration was often too short for its presence to be detected [33] The substance

of eight other papers on this subject is that even after *rigor mortis* has set in and irritability is gone, perfusion with fresh warm blood, preferably well oxygenated can for a time so restore irritability that muscles once more respond to artificial stimuli In other words he had shown that *rigor mortis* occurs under conditions in which there certainly cannot have been coagulation of the protein, that it occurs in muscles which can be said to be still "living," and that it can be temporarily abolished by appropriate procedures He was not a chemist, as was Bernard, and therefore he gave no information as to the chemistry of *rigor mortis* although he stated that the changes were chemical in nature The relation of lactic acid to rigor mortis was not to appear until the beginning of the 20th century when Fletcher (1873 1933) and Hopkins (1861——) devised a special cold technique for handling muscles in order to extract the acid from them quantitatively

To the present writer the most neatly reasoned of all Brown-Séquard s papers of this period is the very short one on strychnine [34] Magendie had started the work on this violent convulsive poison years before, and although he had concluded that its site of action is mainly the spinal cord, it was thought by later

physiologists, e g, Stannius (1808-1883), that its chief action was on sensory nerves, since the poisoned animal jumps madly at the slightest stimulus, even a breath of air Brown-Séquard tied the dorsal aorta in a frog at a point just before this artery bifurcates to descend into the hind legs He then gave the frog strychnine by mouth The ensuing convulsions involved all four legs in spite of the fact that the hind limbs were getting no blood If, however, he transected the spinal cord first and then cut the small arteries passing from the aorta to the spine, before giving the frog strychnine by mouth, there were no convulsions of the hind legs, although for many hours they remained responsive to pricking, pinching and the like, and reflex action involving the cord was therefore still possible In the first experiment it will be seen that the sensory nerves to the hind legs had *received no strychnine while the cord did*, and there were convulsions In the second experiment the sensory nerves of the hind legs received strychnine, but the cord did not, and there were no convulsions The conclusion that strychnine acts on the cord, not on the sensory nerves, is inescapable One needs to be a clever experimenter to repeat this operation on a frog Incidentally, the experiment is the exact

parallel of Bernard's to show that the site of action of *curare* is not nerve or muscle but the myoneural junction between the two. It is not improbable that Brown-Séquard used the *curare* experiment as a model for his experiment with strychnine. I have found no other paper by Brown-Séquard which so closely follows a pattern typical of the way in which Bernard planned an experiment.

There are several other cases in which Magendie's work provided a starting point for Brown-Séquard. In the opinion of his contemporaries, Magendie had weakened his claim to the discovery of the law of direction of conduction in the spinal nerve roots by saying (and quite correctly too) that stimulation of the dorsal roots not only gave evidences of sensation but produced movements as well, and that stimulation of the ventral roots gave evidences of pain as well as movement. The latter phenomenon had received the name "recurrent sensitivity," and Brown-Séquard tried to explain it on the simple assumption that the pain was the result of stimulation of sensory fibers within muscles contracting violently upon application of the electric current to the ventral roots of the spinal nerves.[30] This is an ingenious explanation, but no experimental proof

was offered The problem was solved when Bernard showed that sensory fibers from the dorsal roots double back for a short distance to run along with the ventral roots, so that stimulation at this point affects not only ventral but dorsal root fibers

In 1824 Magendie had shown that trophic disturbances in the eye result from cutting the trigeminal nerve Brown-Séquard reported that transverse hemisection of the cord at the level of the 10th dorsal vertebra would cause similar trophic disturbances, particularly corneal opacities, in the eye of the guinea pig on the side of the lesion [86] Unfortunately the cases which he observed must have been chance coincidences Chance corneal opacities are not uncommon in inbred guinea pigs He should have suspected these observations because he reremarked that it was in fact " bizarre " that he had never seen opacities in both eyes when the cord was completely transected

Another observation following on his often repeated operation of hemisection of the cord was that it led to congestion and increase in size of the suprarenal bodies This is the first record of the direction of his attention to these important organs [87] Pres-

ently they were to be the subject of some of his most brilliant experiments.

Magendie (and also Flourens and Longet) had made the observation that lesions in certain parts of the nervous system, particularly in the region near the cerebellum, would cause the animal to turn in circles or to roll over and over. With Martin-Magron, Brown-Séquard reported that similar results could be obtained by pulling the facial nerve out by the roots.[8] Later[9] he described forced movements half way between rolling and turning as a result of piercing the cranium with a needle in such a way that it passed through the left cerebral hemisphere, the corpora quadrigemina, and the mamillary body. This was similar to Bernard's procedure in conducting the famous "piqûre" experiment of puncturing the floor of the fourth ventricle of the brain, but Bernard's results were more startling and infinitely more important, since he had found that rabbits so treated developed glycosuria.

When Brown-Séquard tried to repeat Flourens' experiments on slicing the medulla to locate the respiratory center, his work was less precise and merely showed that removal of parts of the brain anterior and dorsal to the medulla lead to asphyxia,

and that therefore the region of the brain near the pons and cerebral peduncles is necessary for respiration We shall see that he modified his ideas on this point later

One of the most striking discoveries in the history of physiology was that of Ernst (1795-1878) and Eduard Friedrich (1806-1871) Weber in 1846 (although Bernard also laid claim to it),[40] viz, that stimulation of the vagus nerve leads to stoppage of the heart Heretofore stimulation of nerves had always given rise to positive action of some sort, in this instance it led to cessation of motion This seemed too radical a departure from recognized physiological laws for many physiologists to credit Longet in particular took this attitude When he tried the experiment himself he was unable to obtain the striking results reported by the Webers, by Moritz Schiff (1823-1896), and by other German investigators who successfully repeated the original experiment Brown-Séquard endeavored to set him right[41] In the first place, he thought Longet had not used the right kind of stimulus, and in the second, neater results could be obtained on frogs than mammals He proceeded to demonstrate before the *Société de Biologie* just how wrong Longet was and how right

the Webers were Later he was able to prove that Schiff was wrong in his claim that the heart beat was dependent on the presence both of the vagi and the spinal cord, and that frogs die if the vagi are cut Brown-Séquard demonstrated that frogs so operated upon will live and the heart continue to beat, and he produced before the *Société de Biologie* two frogs with hearts beating vigorously whose vagi had been cut two weeks before [42]

His work on the iris really added little that was new,[43] but it is of peculiar interest at this present time since he brought up arguments against the theory recently revived by Dr O C Langworthy that changes in the diameter of the pupil are accomplished by vascular changes in the iris He claimed that he had been unable to get any very striking changes in the pupil of recently killed animals by injection of fluid into the arterial system, and he was therefore inclined to think that it was not necessary to evoke vascular turgescence to explain pupillary changes

Finally, his work on reflexes had begun to give him an idea of what we now term summation and facilitation, that reflex responses to the same stimulus will be different under different conditions, depend-

ing upon the state of the central nervous system He had not yet used his own term " dynamogénese " for augmentation of reflexes, but the idea is to be found in the early papers

The influence of the *Société de Biologie* is plainly seen in all this work Nearly every reference is to the minutes of this society One can scarcely imagine how he would have developed at this important and still formative period of his life without the constant stimulus of other keen and critical minds intent, like his own, on biological investigation One is struck by his intimate acquaintance with physiological literature, and it is quite natural that many of his experiments should have had their starting point in the classic work of Magendie, Flourens, and other established physiologists Had he gone earlier to the New World he would never have been able to benefit from the weekly clash of wits with Bernard, Bert (1830-1886), Robin, Rayer and the others Although it is beyond question that there were keen minds among the members of the medical profession in America, there was as yet nothing there comparable to the spirit of physiological investigation so much in evidence in France and Germany at this time Even England, although she might boast of a

Faraday (1791 1867) in the physical sciences, could not compete in the 1850's with France and Germany in the field of pure physiology Brown Séquard had founded his career well, but now he was to leave the congenial atmosphere of the Paris *Société de Biologie* for something quite different

3

His choice of Philadelphia as his harbor of entry into America may have been influenced by sentiment for his father's native city, but it also suggests some knowledge of the history of medical education in this country Philadelphia was the seat of the oldest and most influential medical school in the United States and it was in this city that, shortly after his arrival in June 1852 he began his first American lecture series partly as a means to self-advertisement, but partly also no doubt, in a missionary spirit of bringing physiological enlightenment to the New World Nowhere on this side of the Atlantic was systematic physiological investigation, such as had been the very core of his existence in Paris, carried on Beaumont (1785-1853) had been an isolated phenomenon, and what physiology existed was to

be found in the medical schools, taught as an adjunct to anatomy and disguised under the old Edinburgh title of the Institutes of Medicine, which commemorated Boerhaave's (1668-1738) famous treatise published in 1708 [44] Nevertheless, the profession showed its awareness of what was going on elsewhere in the world, and there proved to be an audience for lectures in experimental physiology The *Philadelphia Medical Examiner* announced that it was ready to publish not only Dr Brown-Séquard's lectures, but any other contributions which he wished to make It is therefore from this source that we learn that not all his time on the way across the Atlantic had been spent in learning English, for he seems also to have been intensely interested in measuring as accurately as possible the temperature of the urine of ten strong sailors, as well as of his own He was careful to note that at the time the ship was passing between the 43rd and 45th degrees of northern latitude

There was not a breath of criticism of his command of his newly acquired language and it is only from later animadversions that we can guess that his listeners made no protests because they did not expect too much The content of his lectures was mainly an account of his own researches They were

introduced by a generalization which might have been, and probably was, derived directly from Magendie's early attack on Bichat's vitalism.[47] Brown-Séquard said

> I think that every tissue possesses its vital properties in consequence of its peculiar organization, and that in a completely developed animal nutrition is the source of the vital properties inasmuch as it is the cause of the maintenance of organization.[48]

Further on, he embroidered the latter half of this doctrine, and gave it a mathematical air, by adding,

> The intensity of the faculty which animal tissues possess of producing vital phenomena seems to be in a direct ratio to the intensity and duration of the nutritive reparation, and in an inverse ratio to the intensity and duration of the existence of the phenomena.

Quite as interesting as the origin of this idea is its use as the organizing principle for the first series of lectures and its apparent influence (something it never had for Magendie himself) on Brown-Séquard's experimental procedure. He stated his disagreement with those physiologists who believed that the nervous centers were the source of the vital properties of nerves, and pointed out that nerves even cut

away from their centres, or muscles from their nerves, for a time retained their vital properties, particularly if the circulation (i e, their nutrition) was maintained His idea of specific organization for individual tissues was quite general and in the case of nervous tissue had no reference to the neurone doctrine, which was not formulated for nearly another forty years It is even possible that we have here the theoretical idea behind those curious experiments on grafting cats' tails to cocks' combs, to which Brown-Séquard did not fail to refer as his lectures proceeded

The historical importance of the publication of Brown-Séquard's American lectures in the *Philadelphia Medical Examiner*, however, results from the appearance in the August number for 1852 of the first report of the second of the three discoveries which give him his prominent place among 19th century physiologists The discovery and its circumstances may be given from this report in his own words [47]

My friend Dr Cl Bernard has recently discovered the curious fact that after section of the sympathetic nerve in the neck, the face on the same side, and more particularly the ear, becomes warmer and more sensible than on the

other side The blood vessels are very much enlarged and a great many are visible which were not so before the operation

I have found that the remarkable phenomena which follow the section of the cervical part of the sympathetic, are mere consequences of the paralysis and therefore of the dilation of the bloodvessels The blood finding a larger way than usual, arrives there in greater quantity, therefore the nutrition is more active Now the sensibility is increased because the vital properties of the nerves are augmented when their nutrition is augmented As to the elevation of temperature, I have seen, as Dr Bernard has, that the ear exhibits, sometimes, one or two degrees Fahr more than the rectum, but it must be remarked that the temperature of the rectum is a little lower than that of the blood, and as the ear is full of blood, it is very easy to understand why it has the temperature of the blood A great many facts prove that the degree of temperature and of sensibility of a part, is in close relation with the quantity of blood circulating in that part

I base my opinion in part on the following experiments If galvanism is applied to the superior portion of the sympathetic after it has been cut in the neck, the vessels of the face and of the ear after a certain time begin to contract, their contraction increases slowly, but at last it is evident that they resume their normal condition, if they are not even smaller Then the temperature and the sensibility diminish in the face and the ear, and they become in the palsied side the same as in the sound side

When the galvanic current ceases to act, the vessels begin to dilate again, and all the phenomena discovered by Dr Bernard reappear

I conclude, that the only direct effect of the section of the cervical part of the sympathetic, is the paralysis and consequently the dilation of the bloodvessels Another evident conclusion is, that the cervical sympathetic send (*sic*) motor nerve fibers to many of the bloodvessels of the head

In a footnote Brown-Séquard pointed out that his experiments demonstrate the contractile nature of blood vessels and that other experiments he had performed showed that the nerve fibers in the cervical sympathetic to these blood vessels of the head had the same origin in the cord as those to the iris of the eye

Three months later, in November, Bernard reported to the *Société de Biologie*

If one galvanizes the divided great sympathetic, all the phenomena produced (by cutting the nerve) are reversed, the pupil enlarges, the opening of the lids is increased The eye comes forward out of the orbit, from the active state it was in, the circulation becomes feeble, the conjunctiva, nostrils, ears, which were red, become pale [48]

It was a distinct shock for him to learn later, that Brown-Séquard had anticipated him in this experi-

ment Bernard had made his first report on cutting the sympathetic nerve before the *Société de Biologie* in December, 1851 He evidently had fears that there might be some trouble over priority for so striking an observation, for he added that at that time he merely wished to date the discovery since the full work was to appear later[49] Just when Brown-Séquard made his observations is not stated, but he had hardly arrived in Philadelphia before the report was given in his June lecture (the publication was two months later), and in spite of Bernard's remark that Brown-Séquard had done the work in America, it would seem more natural to suppose that since he had been in the habit of using Rayer's induction machine on every possible occasion, he must have performed the crucial experiments in his own laboratory before he left France, but had not had time to communicate his results to the *Société de Biologie* The report in the *Philadelphia Medical Examiner* remained unknown to Bernard until Brown-Séquard himself informed him of it the following year

In the meantime another series of lectures was delivered in New York in September and October, and a third series in Boston in November and Decem-

ber They were received with enthusiasm in both cities Their delivery in Boston was advertised by the publication in the local medical journal of the appreciative resolutions passed at a meeting of the students of the Medical Department of the University of New York,[60] and at the conclusion of the Boston lectures (which were given one hour three times a week before a class of sixty physicians and forty-five students), resolutions of thanks were proposed by Dr H J Bigelow (1787-1879) and seconded by Dr Bowditch (1808-1892), and there was an expression of appreciation from members of the Tremont Medical School of Boston

Philadelphia was glad to arrange for an additional series of lectures in the following year, and there seemed to be no lack of fresh and interesting material Among other subjects, Brown-Séquard brought up that long-standing enigma, the cause of the heart beat, with cheerful confidence "The cause of the rhythmical movement of the heart has been heretofore unknown I believe I have discovered it"[61] The theory which he proposed was that the heart was excited to action by carbon dioxide in the blood, a not too plausible one, since every case of death by asphyxia seems to disprove it He would have

replied to this criticism by saying that, as in the case of every stimulant, the concentration was of paramount importance, the proper amount serving as an excitant, an excess as a depressant He had been so struck by the convulsive movements during the early stages of asphyxia, when a certain accumulation of carbon dioxide or other unremoved metabolites does serve as a stimulating agent, that he settled upon the theory that carbon dioxide present in the blood and acting on the nervous system was responsible for such diverse effects as epileptic convulsions and the normal heart beat This became one of his fundamental doctrines, and when pressed for an explanation of almost any physiological phenomenon, he was apt to propose that an accumulation of carbon dioxide must be responsible

When the Philadelphians published a fresh set of resolutions at the conclusion of the 1853 series of lectures, they introduced a note of farewell

Resolved that we take leave of Dr Brown Séquard as our teacher with great regret, not only on account of the many original views which he has presented to us, as the result of his own investigations, and the many useful applications of these views in the improvement of the practice

of medicine and surgery, but on account of his attractive qualities as an amiable and honorable man

Although the American lectures had been an unqualified *succès d'estime*, Brown-Séquard was beset by financial problems in the New World no less than in the Old Immediately after his arrival, it is said that he gave lessons in the French language to eke out his resources Later, in New York, he endeavored to engage in medical practice, but this took the modest form of attending obstetrical cases and delivering babies at five dollars each Whatever remuneration his lectures brought him must have been inadequate for his immediate needs, and they had so far failed in what one might guess was their chief object, to secure him the offer of a post as physiologist in an established medical school The lectures were brought out in book form (his first book) in 1853, in English and under the title, *Researches on Physiology and Pathology* A more immediately rewarding publishing venture resulted from a collaboration on an obstetrical treatise, on which he received an advance royalty and which had a large subsequent sale It has not been possible to identify this book, or to discover the name of the

collaborator, but Dr. Rouret of Mauritius is the authority for its having been the only one of the period which gave a physiological explanation of gestation and of respiration and circulation in the foetus. It was translated into French and ran into several editions.

His lectures in Boston were scheduled to begin on November, 1852, so that we may assume that he had not been in that city much more than a month when on December 17, just before the lectures were to conclude, he wrote a letter to Miss Ellen Fletcher, who is always spoken of as a niece of Daniel Webster, or, more precisely, of that celebrity's first wife, and in this letter he told her the story of all his early struggles as a young student in Paris. The letter has been preserved, and it was addressed to a sympathetic reader for in March, 1853, Brown-Séquard and Miss Fletcher were married in Boston. He was now thirty-six, and for ten years, since his mother's death, had been without domestic anchorage. It would seem that at first he may have contemplated medical practice in New York, for his address five months later was 17 University Place, New York City, when he sent a notice to the *Philadelphia Medical Examiner* that he was leaving America, and would be glad to

carry to the *Société de Biologie* in Paris any books or communications which anyone wished to send, if they would leave them at his house On July 30 he left the United States for France, perhaps to fulfill the natural impulse to show his bride the scenes of his earlier life, perhaps only in flight once more from a practical or emotional crisis

Back in Paris, he at once informed Bernard of his experiments on " galvanizing the peripheral end of the cervical sympathetic nerve " Bernard withheld official comment until in December he read his long memoir on the great sympathetic nerve [52] Here he stated

> While I pursued my experiments in France, Budge in Germany, Waller in England and Brown-Séquard in America, each separately, were employed in looking for the explanation of the phenomenon that I had discovered
>
> On his return to France, M Brown-Sequard claimed as his theory stasis of the blood through paralysis of the arteries, and he announced that he had been the first to see in America that galvanization of the sympathetic leads to cooling of the parts and contraction of the arteries I will not enter into discussion of priority relative to facts, all of which date from the same year, and which were developed immediately as quite natural corollaries of my experiment I congratulate myself only on the urgency

which the experimenters just quoted have felt to follow me in this study on the phenomena of calorification. That proves to me that they have found them important and worthy of interest.

It would be a mistake to detect an overtone of sarcasm, uncharacteristic of Bernard, in the final sentence. Bernard meant just what he said, and Brown-Séquard did not feel—and had no need to feel—that an attack had been made on his claim to an original discovery. Once a scientific observation has been announced in the scientific world, there is no patent on it: anyone is free to repeat, elaborate, or produce evidence in refutation. In 1861, in Brown-Séquard's analysis of his own published work up to that time, he said that in the report of his lecture in the *Philadelphia Medical Examiner* of 1852, for the first time was to be found the demonstration of the influence of the galvanism of the sympathetic nerve on the quantity of blood in, and the temperature of, the parts concerned. He added:

This work was published five or six months before that of M. Bernard and M. Waller on the same subject.[1]

Bernard had a stubborn streak. He remained to the end of his days convinced that there must be

more to this action of the cervical sympathetic than mere vascular changes He thought that there must be separate calorific and frigorific nerve fibers acting directly to change the metabolism of the tissues Time so far has shown that Brown-Séquard was right, and for once at least he was not in second place in competition with his gifted contemporary

Paris proved after all to be just as inhospitable as New York to one who desired above all things to continue experimental work and who was unwilling to spend time in acquiring a medical practice which would provide a livelihood and perhaps something over to support unremunerative activities Parisians were reported to prefer doctors who stayed in one place and were there when you wanted them Another resource suggested itself Brown-Séquard's former pupil, Dr Frédéric Bonnefin, and another Mauritian, Henri Lolliot, had finished their medical training in Paris and were on the point of departure to set up practice on their native island Brown-Séquard decided to sail with them, apparently with the intention of trying his chances as a physician on the small tropical island, where the easy life might give him more leisure for his own experiments There is the suggestion that he was living at an

extreme pitch of nervous tension at this time in the remark of Dr Bonnefin that when Brown Séquard came to see him he rushed in like a whirlwind, refused to sit down, he was very restless, and had scarcely arrived before he was in a hurry to be away again." However, the three medical friends, Mme Brown-Séquard and three other passengers embarked, February 10 1854, from Nantes, on a sailing vessel, *Adolphe Lecourt*, Captain Barnes, with a cargo of livestock and the prospect of a three months passage. Mme Brown-Séquard's impressions of the voyage are preserved in an article which was contributed three years later to the *New York Daily Tribune*. Her comments on the passengers, the weather, the waterspouts and the denizens of the water and the air suggest that she was lively and good humored, in fact, a most agreeable travelling companion. Her interest and solicitude extended even to the cargo. She wrote

Our cargo consisted of mules and cows, it was a very valuable one, as only the most hardy of these animals can bear the long ho' voyage. Five of the cows were of the best Norman breed, and on the eighth day out the most beautiful of them died from the heat. Whom the gods love die young." In the still evening she was consigned

to a watery grave, while the glow-worms of the sea came forth with their silver-lighted torches, almost rivaling the stars in brilliancy, to welcome her

In comparison with this epitaph for the cow, Mme Brown-Séquard's account of the drowning of a sailor is almost restrained

One sad event took place which threw a gloom over the early part of our voyage A severe storm came on about sunset, and increased rapidly We were dashing on 15 knots an hour, through a terrific sea, when a young man fell from the mast, and although two stout sailors tried to save him, it was impossible The captain, being at the helm, immediately put the ship about Hen-coops, &c, were thrown out but all in vain He was the only son of his mother, and she a widow

It cannot be denied that Mme Brown-Séquard occasionally indulged in a cliché

When the small ship reached Mauritius, May 12, an epidemic of cholera on the island was almost at its peak A commission of inquiry subsequently decided that the disease had been brought to Port Louis in a ship which had entered the harbor from Calcutta on March 24 Thirty coolie passengers had died of cholera on the voyage Although the vessel was quarantined, cholera appeared in the colony

early in April (too late for the news to have reached [illegible] to prevent the celebration of the Bonne [illegible] Natal) and had become epidemic by May. Out of a population of one hundred and [illegible] died [illegible] the death [illegible] the [illegible] the [illegible] with the [illegible] himself [illegible]

The [illegible] Dr. [illegible] (17[illegible]) [illegible] could [illegible] Recalled that [illegible] on the [illegible] doctrine of the four humours, which explains the [illegible] in cleansing the blood. Bonne Sequard followed [illegible] in prescribing opium. Always willing to [illegible] himself into [illegible]

according to report he several times swallowed the vomitus of cholera victims, and, on one occasion, feeling the symptoms of cholera overtaking him, he took a huge dose of laudanum He was found doubled up in a corner of his room, almost unconscious, having only strength enough left to gesture for strong coffee Dr Rouget remarks that this occurrence was the probable origin of the rumor that at one time Brown-Séquard tried to commit suicide, a way out which seems quite foreign to his nature He would run away from overwhelming situations, but only to take up the struggle with undiminished zest on a fresh battlefield

At the end of August when the epidemic had abated he was made a member of the commission to investigate the cause of the epidemic, but at the beginning of October he resigned on the ground that he was about to leave Mauritius In his final report on the services rendered at *l'Hospice Ste Marie* he modestly gave credit for its successes to his associate organizer and to the devoted sisters of Charity He himself had assumed responsibility for over two hundred patients, and the mortality had been held among these to 28%, which he considered creditable The municipality of Port Louis, in recognition of his

services presented him with a silver cup and a gold medal the latter inscribed, The inhabitants of Mauritius to their countryman Dr Brown Séquard, in evidence of esteem and gratitude, for services rendered during the cholera of 1854 Mme Brown Séquard received from the women of the colony an Indian cashmere shawl"

During the first two and a half months of his stay in the island Brown Séquard must have been fully occupied by the epidemic but when it was over, he apparently managed to devote some time to experimental procedures However, the resources of the place seem to have limited him to the repetition of some of his earlier experiments, and cocks sporting (this time) rats tails on their combs, and other oddly mutilated animals, let loose together in his backyard, began to earn for him the reputation of a sorcerer among the negroes of the community Even less impressionable islanders found him a little startling A description which dates from the time of this visit to Mauritius says that he was a thin little man his hair bleached and wavy, just beginning to silver The vivacity of his speech, his hurried walk the nervous restlessness of his eyes made him

a strange personality" It took very little time to disillusion him about the possibility of carrying on original physiological research under the existing primitive conditions If he had been interested in natural history, he might have considered Mauritius a superb laboratory, but experimental physiology as he practised it with the aid of the inductorium and other intricate apparatus was out of the question When the news finally reached him that he was offered an appointment in physiology at the Medical College of Virginia in Richmond, he must have been in a very receptive mood His compatriots were impressed Early in October, 1854, when, as a farewell gesture, he gave a public lecture on "Physiology," it was before a large and enthusiastic audience, "the *élite* of Mauritian society," according to the island newspaper At the moment it appeared that the security of an academic appointment would establish Brown-Séquard permanently in America

NOTES

LECTURE I

[1] In this connection a letter of Brown-Séquard (*Boston Med. & Surg. Journ.* [illegible] 1866) has been brought by his daughter, Mrs. [illegible] to the writer's attention. He says: "I ought to add that my father's family in the last century settled in New York and in Philadelphia, and my father, who was born in Philadelphia [illegible] when young [illegible] in the United States Navy. [illegible] on the Navy [illegible] I [illegible] in the medical [illegible]."

[2] [illegible] the Notice [illegible] from Dr. [illegible] Brown-Séquard [illegible]

[3] *Mém. Soc. de Biol.* [illegible]

[4] [illegible] March [illegible] a little [illegible] for the [illegible] and [illegible] been [illegible] Claude Bernard [illegible] in December, 1843 [illegible] Brown [illegible] no time [illegible] Brown, August [illegible] 1846. The [illegible] only 10 [illegible] of the best French [illegible] students have the [illegible].

[5] *Journ. de la Physiol. de l'Homme et des Animaux*, [illegible] 1862.

[6] In an article which appeared just after these lectures were given, T. C. [illegible] (*The Journ. of [illegible] and Med.*, [illegible] 1936) points out that Brown-Séquard [illegible] recorded in his [illegible] diminution in reflex [illegible] immediately after [illegible] the cord and [illegible] recovery, is the first [illegible] description of spinal shock, and that this was four years before Marshall Hall gave the phenomenon its name.

[7] Longet, F. A., *Recherches expérimentales et pathologiques sur*

les propriétés et les fonctions des faisceaux de la moelle épinière et des racines des nerfs rachidiens précedées d'un examen historique et critique des expériences faites sur ces organes depuis Sir Ch Bell et suivies d'autres recherches sur diverses parties du système nerveux Paris, 1841

[8] Brown Séquard, C-E, *Recherches et expériences sur la physiologie de la moelle épinière*, 1846, p 26

[9] *Ibid*, p 29

[10] *C R Acad d Sc*, 23 719, 1846

[11] *C R Soc de Biol*, 1 104, 1849

[12] *Ibid*, 34 23, 1882

[13] *Ibid*, 1 18, 1849

[14] *Archives of Scient and Pract Med*, 1 30, 1873

[15] Bernard, C, *Rapport sur les progrès et la marche de la physiologie générale en France*, Paris, 1857, pp 146, 235

[16] Binet, L, *La Biol méd*, 33 5, 1943

[17] *C R Acad d Sc*, 24 363, 1847

[18] *Ibid*, 24 849, 1847

[19] *Bull Soc philomath*, p 83, 1847

[20] *Ibid*, p 74, 1847

[21] *C R Acad d Sc*, 25 482 & 508, 1847

[22] *C R Soc de Biol*, 1 15, 1849

[23] *Ibid*, 1 160, 1849

[24] *C R Acad d Sc*, 29 672, 1849

[25] *C R de Biol*, 1 192, 1849

[26] *Ibid*, 2 33, 1850

[27] *Ibid*, 2 70, 1850

[28] *C R Acad d Sc*, 31 700, 1850

[29] *Mem Soc de Biol*, 7 27, 1855 Cf Olmsted, J M D, The Aftermath of Charles Bell's Famous 'Idea, *Bull Hist Med*, 14 341, 1943

[30] *C R Acad de Sc*, 32 897, 1851

[31] Vulpian, A, *Leçons sur la physiologie générale et comparée du systeme nerveux faites au Muséum d'histoire naturelle* Paris, Baillière, 1866, p 459

[32] *Med Exam Phila*, 8 560, 1852
[33] *C R Soc de Biol*, 1 138, 1849
[34] *Ibid*, 1 119, 1849
[35] *Ibid*, 2 171, 1850
[36] *Ibid*, 2 134, 1850
[37] *Ibid*, 3 146, 1851
[38] *Ibid*, 1 133, 1849
[39] *Ibid*, 3 79, 1851
[40] Bernard, Cl, *Rapport* , Paris, 1857, pp 66, 195
[41] *C R Soc de Biol*, 2 26, 1850
[42] *Ibid*, 2 45, 1850
[43] *Ibid*, 1 116, 1849
[44] Cf *Science in the University*, Univ of Calif Press, 1944, p 293
[45] Olmsted, J M D, *François Magendie*, Schuman, N Y, 1944, pp 29 33
[46] *Phila Med Exam*, 8 481, 1852
[47] *Ibid*, 8 489, 1852
[48] *C R Soc de Biol*, 4 169, 1852
[49] *Ibid*, 3 163, 1851
[50] *Bost Med & Surg Journ*, 47 338, 1852 The notice in the New York *Tribune* of a meeting of the students of the Medical Department of the University of New York, Oct 18, 1852, is quoted, including the resolutions passed on that occasion

Whereas, The successful practice of the Healing Art imperatively demands a knowledge of the functions of the various organs of the animal economy, which branch of medical knowledge has been too much neglected, but is now justly engaging the attention of, and becoming properly appreciated by the Profession, and *Whereas*, Dr Brown Séquard, of Paris, in his experiments and investigations for the advancement of Physiological science, has arrived at conclusions, and rendered truths demonstrable, which have been heretofore unknown or conjectural—Therefore,

Resolved, That Dr Séquard is entitled to the commendation of the Medical Profession, and merits their approbation, and further,

Resolved, That we hereby tender him our sincere and heartfelt thanks, as an humble testimonial of our appreciation of his instruc tion and interesting series of lectures before the class

'*Resolved,* That while our thanks are eminently due to Dr Séquard, they are no less due to the Faculty of the University for his introduction to the class, as well as for their untiring efforts in sustaining in an able and superior manner the past summer s course of Lectures

Resolved, That we hereby tender them our most hearty thanks

[51] *Phila Med Exam*, 9 504, 1853

[52] *Mém Soc de Biol*, 5 77-107, 1853

[53] *New York Daily Tribune,* June 27, 1857, p 6

[54] Brown Séquard s daughter, Mrs McCausland, still possesses the medal and the shawl, but denies all knowledge of the cup, which is nevertheless mentioned in the mayor s letter of presentation Rouget, *Renseign suppl*, 6 7

LECTURE II

HIS NEUROLOGICAL PRACTICE AND AMERICAN PROFESSORSHIPS

I

THE Medical Department of Hampden Sidney College in Virginia had for some years been located in Richmond. Although by the charter of the institution its trustees had the right to appoint its professors, the faculty itself had, to all intents and purposes, made its own appointments, since the trustees had always acquiesced in their choice. In 1853, however, unfortunate jealousies came to the surface, and when a certain candidate for the newly proposed chair of Physiology and Medical Jurisprudence, who had been selected by the faculty, was turned down by the trustees in favor of a candidate of their own choosing, insurrection broke out. A bitter contest followed in which the opposing forces employed "the most venomous invective that printers would publish."[1] The result was that the rebellious professors severed their connection with Hampden-

Sidney, took the quarrel to the State legislature, and were granted a charter of their own under the name of the Medical College of Virginia, February 25, 1854 One of the first acts of the "Visitors," whom the State legislature had appointed for the governance of the institution, was the confirmation of the desirability of establishing a Professorship of the Institutes of Medicine and Medical Jurisprudence The newly constituted Medical College of Virginia therefore voted, May 25, 1854, on candidates for the new chair Seven names were proposed, among them that of Brown-Séquard, who had met influential members of the medical profession in Richmond at the meetings of the American Medical Association in 1852 The first vote was 11 to 2 in his favor On learning this result the two supporters of another candidate transferred their votes, making the appointment unanimous

The decision to call Brown-Séquard to Richmond was publicized in one of the Virginia medical journals as follows

M Brown Séquard is probably not as well known to the medical men of our State, but we are well satisfied that there is not one of the candidates for the physiological chair (if he is familiar with the science he is anxious to teach)

who can dispute the propriety of the appointment The department of medicine has had new and brilliant light thrown upon it by the indefatigable researches of this gentleman In the great field of experimental physiology, M Sequard and his celebrated co labourer and rival, M Claude Bernard have gained equal reputation M Bernard, in reward for his investigations has recently been appointed to the new chair of general physiology in the Faculty of Sciences at Paris What more fitting compliment could we pay Dr Séquard, American as he is on the maternal (*sic*) side, and desirous of giving to this country the fruits of his future researches, than to select him for this position in our own College, for whose prosperity the Virginian profession should earnestly labor and which we hope to see worthy of the State which has given it birth [7]

The inevitable comparison with Bernard recurs in a review of Brown Séquard's recently published lectures, *Researches on Physiology and Pathology*, which appeared in the same journal

This book presents the results of a most careful experimenter whose contributions to physiological science are most valuable Although his researches are not as brilliant as those of his compeer Bernard, they are more extensive, and we may add that his results are less controverted [8]

This judgment is not so much balanced as balancing upon a tight rope It was perhaps true that Bernard's

work had provoked more opposition than Brown-Séquard's, if only in proportion to the greater significance of some of it

When communications were established by the Virginia authorities with Brown-Séquard's friends in Paris, particularly Broca, the College was assured that the appointee would certainly accept when notice of the offer could reach him in far-away Mauritius Broca's letter is illuminating where it gives reasons for his friend's lack of success in France He wrote

> He is not a Frenchman, although educated in Paris, and speaking the language like one of us, although acknowledged to be possessed of eminent talent, he has nevertheless been unable to attain any official position, only because he is a foreigner

Some Virginians, too, had objections to a foreigner, for the editor of the *Virginia Medical & Surgical Journal*, in announcing Brown-Séquard's appointment, snapped,

> We are striving to build up a great College in Virginia, not to make fat offices to put our friends in We look around for the *best* man to fill a professorship, and we take him, whoever he is

Some idea of what actually happened when, after

all this fanfare, the "eccentric genius" (for that in the end was the impression he made on the College) finally arrived in Richmond late in the autumn of 1854, may be gathered from the reminiscences of one of his pupils, Dr William H Taylor (1835-1917) "To begin with, there was already disappointment that the renowned acquisition had not stimulated enrollment to the degree that had been anticipated Language difficulties arose According to Dr Taylor, Brown-Séquard's "discourse was not very unlike an attack of spasmodic asthma, and frequently his agony in trying to make himself comprehended was, if anything, greater than ours in trying to comprehend him" There seems to have been no plan to provide material for physiological demonstrations, but the students were most cooperative in this matter and ranged the town and the adjacent countryside collecting a menagerie of dogs, cats, raccoons, terrapins, and other available animals, which were all quartered together in the cellar of the so-called Egyptian Building which originally housed the Medical College The resulting animal noises, ascending from beneath, accompanied lectures in the daytime and prevented sleep for the resident students at night The janitor and his wife were

particularly distracted The students were impressed by the demonstrations on living material, but did not always understand them, as often as not viewing them "with pleased astonishment," as if they were "wonders wrought by the stage magician" It was felt that the new professor, in spite of the conscientiousness with which he insisted on demonstrating even the obvious, frequently talked over the heads of his hearers It was complained that he lacked administrative ability, energy (although what this could have meant as applied to Brown-Séquard is a little hard to understand), and displayed "a surplus of honesty"

His frankness was most displeasing when he used it to express the very great repulsion which he felt to the idea of slavery The equalitarian principles which triumphed in the French Revolution were strong in him, and in Mauritius the negroes who made up the majority of the population had long since been made free He felt so keenly and was so outspoken on this subject that it began to be whispered that coming from Mauritius and having a dark complexion he must himself have negro blood In Virginia there could be no surer way of discrediting a man than to hint that he had tainted blood

He was not equipped for social success either The story is told that on one occasion while in the United States he was staying with friends in Baltimore, and his hosts wished to give a party in his honor They invited guests to meet the celebrity on a certain evening, but when the company was assembled, to the embarrassment of all, it was found that the great man had retired at his usual hour of 8 p m and refused to come down

On his own side Brown Séquard had grounds for disappointment No suitable installation for experimental physiology had been provided, and his own researches were not progressing It is true that Dr Taylor professes to remember holding cats 'by the tail ' while the professor ' worked his way into their interiors," but this seems a very unusual, not to say dangerous, technique in animal experimentation, and probably brought the operators nothing but lacerations On one well-remembered occasion, Brown-Séquard evidently following up experiments of Magendie on the functions of the skin, and using himself as experimental material, varnished his skin completely, even including his face, with a coat of sticky impervious material, and was presently found by a student lying unconscious on the floor of the

animal quarters in the College basement The student, with presence of mind, removed the varnish with alcohol (or, according to a less credible report, with sandpaper), and saved the life of a scientist The grafting experiments were not neglected, but, if Dr Taylor's recollection serves him, varied by the use of a dog's tail, and the story of the cock which lost its unnatural crest in battle was retold

A more understanding account of Brown-Séquard's researches while he was in Richmond, together with an appreciation of his personal characteristics, is given by the editor of the *Virginia Medical and Surgical Journal*, Dr J B McCaw (1823-1906) who later became dean of the College He wrote

I was very intimate with him (Brown-Séquard), and worked with him in many of his vivisections He was the most expert operator on the living subject I ever saw, and his dogs, rabbits and guinea pigs were cauterized and handled in the most artistic way He was mostly engaged with a comparison between the drug, opium, and the new bromides, chloral and that class of remedies By trephinating the skulls of guinea pigs he studied the effects of opium and narcotics on the dura mater Alternating with chloral and bromides he proved that the opiate always engorged the membranes of the brain, while chloral bleached the dura mater

Ever since that time the profession has recognized the fact and acted upon it, as in the sudden convulsions of children and the uremic convulsions of Bright's disease

The enthusiastic nature of Brown Séquard shows us his whole life and bearing Simple minded and guileless, he was truth itself as far as he saw it His most affectionate nature made dear friends wherever he was[5]

Although, as this shows Brown Séquard had won some esteem from his associates, the post in Richmond was uncongenial to him He had no desire merely to cram students for examinations, or to be associated with members of a faculty who did not have as their unremitting aim in life the prosecution of experimental research He could have been really happy nowhere in the United States, either in this pre-civil war period, or for another quarter century, until sufficient interest in original investigation would be aroused to instigate the founding of the American Physiological Society in 1887 In spite of his British citizenship, Paris was the place for him It is therefore not surprising that at the end of one term he sent in his resignation and its acceptance is recorded in the minutes of the Board of Visitors on March 30, 1855 The record book of the Faculty mentions only that he attended several faculty meetings and

was one of the delegates appointed to attend the American Medical Association meeting in Philadelphia, beginning May 1, 1855 After filling this engagement and spending a short time in New York, he sailed back to France His stay in the American South had had no effect on his fortunes whatever, although his friends in Paris were moved to comment on the coat of tan he had acquired in that latitude

2

His return to Paris and the consequent reunion with his scientific confrères in the *Société de Biologie* precipitated a crisis in the long-standing and bitter discussions of his doctrines regarding the crossing over of sensory impulses in the spinal cord, which had been going on since his crucial experiments of 1849 According to Broca in the famous report read before the *Société*, July 21, 1855, Brown-Séquard had demanded a show-down "He considered," Broca said, "that it was time to put the *Société de Biologie* under the necessity of pronouncing on the most fundamental question of the physiology of the nervous system" The committee charged with reviewing the question included, besides Broca, Cl Bernard,

Vulpian, and three less well-known members The verdict, as presented by Broca, was an overwhelming vindication of the conclusiveness of Brown-Séquard's experimental results, and established his reputation as an authority on disturbances of the nervous system, both from the standpoint of the laboratory and the consulting-room

This victory permitted his next enterprise to begin under favorable omens Jointly with the friend of his youth, Charles Robin, he established in 1855 a small laboratory in the *rue Saint-Jacques*, where he worked at his own researches, and at the same time took pupils who came to carry out experiments, mostly on the nervous system Some of these, who later became very well-known in the medical world, were I Rosenthal (1836-1915), later professor of physiology in Berlin, K F O Westphal (1823-1890), later professor of nervous and mental diseases in Berlin, J N Czermak (1828-1873), who became professor of physiology first in Prague and then in Leipzig, and J J A Laboulbène (1825-1898), eventually professor of the history of medicine in Paris Work with students in what we should call their " graduate " phase was much more congenial than elementary demonstrations in the Medical Col-

lege of Virginia, and the new venture was successfully maintained for two years, Brown-Séquard's lively spirits and engaging personality, no less than his reputation, proving an attraction to disciples

In October of 1855, Magendie died, and there were thus two important vacancies created, a seat in the Academy of Sciences and the professorship of Medicine in the *Collège de France* Through a mistake in the minutes of the Academy of Sciences, it is made to appear that Brown-Séquard asked to have his name put on the list of candidates for both positions In reality he had applied only for the professorship Even without a comparison of their scientific achievements, he stood no chance against the favorite candidate, Claude Bernard, his own lack of French citizenship being against him, and sentiment being all on the side of Bernard The latter had for years served as Magendie's substitute, and the old professor on his deathbed had so far as was in his power bequeathed his chair to his able assistant It was therefore Claude Bernard's name, with Longet's as alternate, which was sent by the Academy of Sciences to the Minister of Instruction for approval

The chairmanship of the committee to award the

Montyon Prize in Experimental Physiology, which had long been Magendie's prerogative, carrying with it the repeated bestowal of the prize on Bernard, now, as might have been predicted, fell to Bernard himself. Brown-Séquard had submitted papers for this annual prize not once, but four times, beginning in 1850, and each time had had to be content with honorable mention, Bernard on two of the occasions walking off with the [illegible] prize. The first award made by the committee under Bernard's chairmanship [illegible] to Brown-Séquard for his work on the [illegible] of sensory impulses in the spinal cord.

Bernard [illegible] most illuminating. He [illegible] the demonstrations Brown-Séquard had performed under the [illegible] for in one place he refers to [illegible] which the [illegible] physiologist [illegible] committee, and in another to [illegible] in the presence of the [illegible] Brown-Séquard [illegible] results. The [illegible] all. In [illegible] with [illegible]

cut through the posterior columns, and demonstrated that a pinch on the hind limb was evidently experienced as pain by the animal, and that the cord both anterior and posterior to the cut was still sensitive, in another similar preparation a transverse cut through the whole cord except the posterior columns, which were left intact, abolished perception of pain from the hind limbs, in still another, he demonstrated that sensory impressions were conveyed in the gray matter of the cord, not in the white Bernard concluded his report by saying that Brown-Séquard had shown that the pathways of sensory impressions from the cord to the brain were more *complicated* than had formerly been thought There is no mention of their crossing in the cord Is it possible that Bernard still (and in spite of Broca's championship) did not believe that Brown-Séquard had fully demonstrated this fundamental point? To us, the proof of sensory crossing, rather than demonstration that the posterior columns do not convey all sensory impluses, is the important feature of the whole work

The stimulus of interchange of scientific ideas in the *Société de Biologie* (of which Brown-Séquard now became a vice-president) and opportunity for work in his own laboratory bore fruit before the end

of this year, 1856, in the third of his best-known contributions to physiology, viz., the effects of extirpation of the suprarenal bodies. It is strange that in listing his own publications in chronological order he gives as his first reference to this important piece of experimentation not the two papers read before the Academy of Sciences in the autumn, but a letter he wrote to the Academy of Medicine answering objections to his work as it had been reported to that body by Trousseau. It appears that Brown-Séquard's own reports before the Academy of Sciences treated the subject as a matter of pure research on lower mammals, while Trousseau on the day following this report gave a *resumé* of it at the Academy of Medicine emphasizing the application to human patients. It is true that what had started the research eight months earlier was a book published the year before by Thomas Addison (1793-1860), physician at Guy's Hospital in London, in which he described a peculiar disease to which he gave the name "bronzed disease," or as it appeared in some of the French reports, "Bronzed Skin." Trousseau added in an aside in his report that in his opinion "this condition should be given the name Addison's Disease, attaching henceforth to this affection the name of him who

discovered it" This has been done Addison showed that the peculiar bronzing of the skin sometimes seen in patients was found at autopsy to be related to pathological changes in the suprarenal bodies Brown-Séquard's experiments took up the story at this point, and demonstrated the importance for the life of a mammal of the presence of these small bodies which had been neglected by physiologists, in spite of some good histological work by Rayer some twenty years before [6]

The striking phenomenon which Brown-Séquard had discovered and reported to the Academy of Sciences, August 25, was that the lower mammals died, usually within twelve hours, after extirpation of the suprarenal bodies The symptoms appearing after their removal were gradual muscular weakening, which became very marked toward the end, more rapid respiration at first, which later became notably diminished, irregular and gasping, a heart-beat enfeebled but more rapid than the normal state, and a fall of body temperature In the last moments of life there were vertigo, rolling over, and convulsions Blood from a healthy animal injected into the veins of an animal deprived of its suprarenal bodies caused the latter to survive several hours longer than

it would otherwise have done In trying to find the cause of death he was convinced that neither hemorrhage, peritonitis, damage to neighboring viscera nor interference with the great sympathetic nerve, which sends fibers to the suprarenal bodies, could be responsible The blood of animals deprived of suprarenal bodies seemed to be charged with a toxic principle, since when it was injected into an animal with one suprarenal body missing, death was hastened His final conclusions were· (1) these organs are essential to life, at least for cats, dogs, rabbits and guinea pigs, (11) ablation of them leads to death even more rapidly than removal of both kidneys, (111) these organs have numerous relations with the cerebrospinal centers His general conclusions were valid, but improvement in technique has resulted in longer periods of survival than he thought possible [7]

Since Trousseau included important points not mentioned in Brown-Séquard's first report, he must have seen not only the manuscript of this report but also that of the second communication to the Academy of Sciences, and a third report as well, which was a complete account of all the experimental work and appeared in October in the *Archives générales de médecine* These points were Contrary

to prevailing opinion, the suprarenal bodies were not exclusively embryonic structures, since they gained in weight and size from birth to adult maturity in man as well as in animals, as an alternative theory to the presence of a toxic principle in the blood to account for death it was now proposed that with the suprarenals removed some property was lacking to the blood which was ordinarily supplied to it by these organs, it had been noted that Parisian rabbits often suffered from a fatal epizootic disease, in which they exhibited the same symptoms as rabbits after removal of the suprarenals, and that at autopsy these organs in the diseased rabbits always appeared inflamed, and, finally, the parallel between these diseased rabbits and patients suffering from Addison's disease was pointed out

This is quite a complete account of the phenomena It shows unusual powers of observation and ability to cope with physiological problems to have been able to accomplish so much in a short eight months of experimentation The work is a classic landmark in endocrinology, and further real advance in our knowledge of the functions of the adrenals was delayed until 1894 when Professor Schafer's (1850-1935) scepticism in regard to Dr Oliver's (1841-

1915) extravagant claims for the action of an extract of these bodies led to the opening of the modern phase of the science."

The attitude of some of Brown Séquard's contemporaries is shown in the interchange between Trousseau and one of the members of the Academy of Medicine. When Trousseau had made his report, he had added, after describing the experimenter's finding on his rabbits, cats, dogs and guinea pigs, that he himself had examined a hospital case of bronzed skin. The patient died and after the autopsy Trousseau had sent the suprarenal bodies to Brown-Séquard for microscopic examination. There were found in them tuberculous deposits, some 'cretaceous matter!' (the exclamation point is Trousseau's), and a fluid resembling pus, with, however, very few leucocytes. This was excellent confirmation of the applicability of Brown Séquard's findings to the human patient. In response to Trousseau a Dr Bouillard demanded the floor to say that he was struck by two things in the report, first, the clinical facts cited, and secondly, what he could only term the philosophical prologue. The clinical part seemed intensely interesting and of significance, but he saw "in the experiments of M. Brown-Séquard nothing

more than what one might call amusing physiology" It was in defence of this "amusing physiology" that Brown-Séquard replied in his letter to the Academy of Medicine He said,

> If this estimate touched only myself, I should have kept silent, but the remarks of M Bouillard, if I have understood their import, tend to nothing less than the denial of the value of a great method of scientific investigation [9]

It was the old debate over the value of animal experimentation, which had been raised against Magendie and Bernard, and which was not a dead issue in 1856, if indeed it can be said to be so in 1946

If Brown-Séquard had abandoned his experimental research at this point, his fame as a physiologist would still have rested secure If he had never done more than show the effects of hemisection of the cord, the effects on blood-vessels of stimulation of the cervical sympathetic nerve, and the effects of removal of the adrenals, he would still rank among the world's notable physiologists In spite of being engaged in incessant experimentation until the very end of his seventy-seven years, he had already accomplished his major work before reaching the age of forty Much that he did later was spectacular and

of significance in that it started trends in physiological experimentation, but in terms of actual achievement he had made his real contribution to physiology by 1856. This is not to say that his subsequent work was not useful, but he was never again to make a strike comparable to those he had already made.

One way of expressing the change in his attitude, a change which will become obvious as we proceed, would be to say that about 1856 he ceased to be a "pure" physiologist and became an "applied" physiologist, thus losing a halo and acquiring a forked tail, or *vice versa*, according to one's point of view.

3

The subject which now began to claim his overwhelming interest was epilepsy. As he had successfully tied up his work on the suprarenal glands of animals with Addison's disease in human patients, he now made application in his private medical practice of the results which he had obtained in his experimental work on "artificial epilepsy" in guinea pigs. This work was the rather curious sequel of his experiments on hemisection of the spinal cord, for many of the guinea pigs with operated spinal

cords were kept alive for months, and some of them developed a peculiar epileptiform disease characterized by periodic convulsions Measures which he had found effective in alleviating symptoms in the guinea pigs he began to apply to human cases He was increasingly in demand as a physician, particularly in this field of epileptic seizures, and he presently acquired a *clientèle* in Paris, which, if cultivated, would have provided him with ease, if not with actual wealth However, he did not have the temperament of a successful city practitioner He was an indefatigable experimenter, and he also enjoyed telling other physicians and scientists about his work We therefore find him in 1856 neglecting his practice in Paris to give a series of lectures on epilepsy in Boston A copy of the customary congratulatory resolutions at the close of a series is to be found in the *Boston Medical and Surgical Journal* of December 4, 1856 This journal had begun to print the lectures the month before When the whole series had been published in this way, they were brought out in book form in the next year under the title, *Researches in Epilepsy, its Artificial Production in animals, its Etiology, its Nature and its Treatment in Man*[10] It is just possible that Mme Brown-Séquard

may have proposed this visit to America in order to display to her own family her first born. An only son, Arthur Désiré-Jules Charles Édouard was born February 19, 1856, at 30, rue Monsieur le Prince, Paris.

In the Boston lectures Brown-Séquard stressed particularly his concept of the "aura epileptica," a portion of the body differing in location in different individuals, which seemed closely associated with the setting off of convulsive seizures. He had found the region about the face and neck of his epileptic guinea pigs to constitute such a zone, and in one of his patients he had found a spot on the arm near the bend of the elbow, and in another an area on the skin of the neck where application of the electric current would incite convulsions of the whole body. He suggested that the mechanism was as follows: certain nerve centers were extremely sensitive (they were more likely, he thought, to be located in the spinal cord than in the brain) and the presence of carbon dioxide in the blood flowing through these areas served as a stimulus to set off impulses of nervous force from these unduly sensitive areas, which finally culminated in a general convulsion. It is here that his theory of "action at a distance"

played a prominent role, for he thought that even though irritation of the cutaneous filaments of certain sensory nerves could set off a convulsion, the nervous center directly concerned with production of a convulsion might be located almost anywhere in the whole cerebro-spinal system As for curative measures, he advocated some form of treatment which would break the connection between the site of the "aura" and these sensitive nerve centers Recourse might be had to cutting of nerves or even amputation, which he had used in his experiments on guinea pigs

A recent treatise on epilepsy[11] dismisses this type of the disease, the so-called "Brown-Séquard" or "spinal" epilepsy, with the comment that a convulsion set off in a guinea pig through stimulation of the skin after injury to the spinal cord is nothing more than a vigorous scratch reflex, as was shown in 1909 by T Graham Brown[12] We shall see later on how beautifully this explanation of "artificial epilepsy" in guinea pigs fits in with the results of a recent re-investigation of this subject Brown-Séquard's whole concept of the disturbance was based on a false foundation He was blinded by a superficial resemblance of guinea pig symptoms to symptoms

appearing in human epileptics and did not arrive at the true cause of the disturbance in his experimental animals

In July, 1857, it was announced in the medical journals that the celebrated physiologist intended to leave Boston to proceed immediately to Paris to superintend the publication of a work on the brain and spinal cord, but that he was to return in the fall to occupy a chair as Professor of Physiology at the Cooper Institute in New York, to which he had already been appointed The notice further stated that for the fourth time Brown-Séquard had been awarded the Queen's Prize (£100) from funds of the Royal Society of London By October, however, he had resumed his practice in Paris, evidently having refused the New York appointment, and was busy reading papers and discussing his results on artificial epilepsy at scientific meetings

The Royal College of Surgeons, London, invited him to deliver a series of six lectures on the physiology and pathology of the nervous system These lectures were given in May, 1858, and were first published in the *Lancet* After being expanded, they were also brought out in the United States as a book, *Course of Lectures on the Physiology and Pathology*

of the Nervous System [13] The volume was dedicated under the date September, 1860, to two friends, H J Feltus [14] of Philadelphia and Jules Chauvin of Port Louis, Mauritius, in these words,

My dear friends, Had it not been for the assistance I owe to your extreme kindness, it is probable that the publication of the present edition of these lectures in book form, would have been much delayed, I therefore take, with great pleasure, this opportunity of publicly expressing to you my very best thanks

In the autographed copy which he sent to his boyhood friend in Mauritius he added,

À Jules Chauvin La dédicace ci-dessous n'exprime que faiblement mes sentiments envers toi

It seems odd that at this stage of his career any assistance towards publication would have been necessary

The preface, dated from 81 Wimpole Street, Cavendish Square, W , London, defines the scope of the work

These Lectures contain the results of the work of almost all my life, since I began to study medicine From the year 1838 to the year 1858, when I had the honor of delivering them at the Royal College of Surgeons, in London, and ever

since, I have devoted all the time I could to the study of the great questions the solution of which I have tried to give in these Lectures If I have not succeeded in my endeavors, I can at least have this consolation, that it is not merely because I have proceeded hastily But, however prolonged my researches have been, I am afraid that I must have come to erroneous conclusions on several points, because the questions discussed in these Lectures are as difficult as they are important, and also because many of these questions are quite new, and I had not, therefore, the views of other authors to guide me I will be thankful to anyone who will show me on what points I have erred

The first of the lectures is of special interest because in it he announced a principle which was to determine the pattern of his work for the remainder of his career, that animal experimentation must be checked by reference to human pathological cases and *vice versa* As he put it, ' Great advances in the medical sciences are due to the combined use of vivisections and clinical observation " The lectures draw upon both sources Nothing more need be said of them here, except that the major points of lasting value have already been dealt with, and it would be unprofitable to point out *all* the " erroneous conclusions " in spite of the courteous invitation to do so

In emulation of Magendie, Brown-Séquard at his

own expense in 1858 started publication of a scientific journal It was published in French and in Paris under the title *Journal de la Physiologie de l'homme et des animaux* It is often referred to simply as " Brown-Séquard's Journal " He began his first issue with a formulation of twelve " laws relative to the dynamic phenomena of animal economy," the point of which was the dependence of " vital " phenomena upon the restorative processes of nutrition and upon conditions of the environment, e g , temperature The idea was the same as that of the manifesto with which he began his first American lectures One department of the *Journal* was devoted to an account of the " progress of physiology " as represented by abstracts of current medical literature The first example was an account of a hanging in Boston with particular reference to the final movements of the victim's heart This had probably caught the editor's eye because of his own spectacular experiments upon the cadavers of executed criminals, and while the observations are interesting, they scarcely contributed to the progress of physiology Bernard expanded one of his reports to the Academy of Sciences, and Charles Robin inserted two original articles, but Brown-Séquard also followed the precedent of Ma-

gendre in the make up of his paper, for the bulk of its pages was filled with his own work.

With the fourth volume 1861, he found the task of editorship too much to carry alone and obtained the collaboration of his former tutor, Martin Magron, and of his particular friends, Robin and Broca, and others as well. Even then the *Journal* was slow in appearing. The sixth and last volume, although dated 1863 actually appeared at the end of 1865 as is shown by a note of December 6 of that year, in which Brown-Séquard apologized to his readers for delays in the appearance of numbers since 1860.

A feature very useful to a biographer is the publication in 1861 of a *résumé* in chronological order of every paper Brown-Séquard had written up to that year. Reference to this list has already been made. During his lifetime several such *résumés* of his work were issued, and they all have an advantage over the bibliography published under the title *L'Oeuvre de Claude Bernard* by that scientist's disciples after his death, in that they are the product of the author's own judgment and indicate what he thought to be the essential feature of each contribution.

The editorship in Paris was interfered with by the demands upon him arising out of his growing reputa-

tion across the Channel Berthelot (1827-1907) says that at this time his influence was perhaps greater in England than in France It rested partly upon his gifts as his own publicity agent In addition to the lectures in 1858 before the Royal College of Surgeons there was a series in the same year at St Bartholomew's in London, and in May, 1859, there is a notice in the *Lancet* that he had just completed a special course of lectures in Dublin He also lectured in Edinburgh and Glasgow, and in Glasgow was made a Fellow of the Faculty of Physicians and Surgeons, and even offered a chair at the University, which he refused because he disliked the climate His medical practice in Paris had been entirely abandoned, and in March, 1860, he was appointed physician at the National Hospital for the Paralysed and Epileptics, which through the instrumentality of the Misses Chandler, one of whom was paralysed, had been established in Queen Square, London, the preceding year Here he delivered lectures for the next three and a half years No salary went with the post, but it did give prestige, and introduced him to a large and profitable English *clientèle*, which he administered from his fashionable Wimpole Street address In 1860 he was elected Fellow of the

Royal Society of London" and of the Royal College of Physicians. In 1861 he delivered the Royal Society's Croonian Lecture and the College of Physicians' Gulstonian Lecture. It is not astonishing that five years of this sort of life brought him to the point of exhaustion.

One of the very bright spots of his London sojourn was his association with J. Hughlings Jackson (1835-1911). Jackson had been serving as House Surgeon to the Dispensary at York when the Hospital in Queen's Square was founded. Already on the staff when he arrived from the north was "that erratic genius," Brown-Séquard (the expression is James Taylor's in his *Biographical Memoir of J. Hughlings Jackson*), and it was he who urged the young man to pursue neurological investigation. Another contemporary, Sir Jonathan Hutchison (1829-1913), says that Brown-Séquard had great influence over Jackson, and told him in no uncertain terms that it was "a waste of effort to spend his time in wide observation of disease in general, if he wished to get anywhere, he had better stick to the nervous system." This suggests a change of front since Brown-Séquard's earlier sojourns in America, where he was several times quoted as protesting against being regarded as

a specialist and insisting that the whole of physiology was, and always had been, his field In any case, Jackson took the advice in the form in which it has been quoted, and later the older man was proud to refer to Jackson as his one-time assistant, even though he could not always agree with him In the world of nervous disease Jackson in time definitely outshone his former chief It is the irony of fate that although Brown-Séquard did institute a form of treatment for epilepsy, the use of bromides (which until the recent introduction of the barbiturates was the most efficacious agent in affording relief to sufferers from this affliction), the types of epilepsy named for him are now considered doubtful, or, at best, secondary diagnoses, and on the other hand "Jacksonian epilepsy" is still at the top of the list as the best-known type in the whole group of nervous disturbances gathered under the head of epilepsy

Brown-Séquard's work at the National Hospital for the Paralysed and Epileptics is acknowledged to have been one of the chief factors in giving it the great celebrity which it attained In recognition of his clinical experience and growing reputation as a neurologist he was asked to contribute a section to the four-volume treatise on surgery edited in 1862

by T Holmes (1825-1907), Assistant Surgeon to St George's Hospital[16] His section was entitled, "Diseases of Nerves," and dealt with epilepsy, hysteria, chorea, paralyses, and the like In the same volume, no 3, we note a section on "Amputation" and another on "Anaesthetics" by Joseph Lister (1827-1912) Brown Séquard was in good company Succeeding editions for the next twenty years retained his section on nervous diseases, that of 1882 having revisions by another author

From hints let drop by such journals as the *Lancet* it may be gathered that there was surprise and even disappointment when Brown Séquard decided in 1863 not to remain in London to continue his services to the unfortunate sufferers from nervous disease The *Lancet* said that his lectures of 1858 had 'altered the face' of neural physiology and pathology, that the lecturer was held in the highest esteem, and that there would be the greatest regret at his departure from a city "where his success as a practitioner was rapid and lucrative beyond precedent, and where he quickly acquired a large circle of warm friends" The reasons given for his leaving were three health (his multifarious activities had exhausted him), family ties (his wife wished to return to her native

America), and his desire to resume physiological investigation The story current in the family is that he looked out one day from the window of the larger house in Cavendish Square to which he had moved in 1863, and saw the Square full of the carriages of people who had come to consult him Suddenly, he felt that he was wasting time as a practitioner and could not bear it He packed up and went to Paris to spend what he had earned on research and pure science, although, in fact, his restless mood did not allow him to stay long in Paris, but carried him within the year again to America

The transference of attention from "pure" to "applied" physiology, which has been remarked in connection with his lectures before the Royal College of Surgeons in 1858 (and which appears even earlier, while he was still in Paris, in his work on the adrenals), had not failed to leave its mark on his scientific output during the busy years of his lectureships and his London practice The true cause of his change of attitude is very likely to be traced to his continued failure to acquire an official academic post in Paris He was obliged against his real inclination to engage in medical practice in order to live, and,

as he could do nothing half-heartedly, the problems which he encountered professionally took increasing possession of his imagination and energies It is intriguing to speculate what would have happened to Claude Bernard if he had not found a haven with Magendie at the *Collège de France* It is to be feared that the world might never have heard of him, and he might have lived out his days as a quiet country doctor Brown-Séquard had personal qualities which prevented him in any circumstances from being condemned to obscurity He had what in our day would be thought of as a flair for publicity One may even recall the frequency with which he took the floor in the early days of the *Société de Biologie* In the London years he actually did manage to continue experiments on *rigor mortis*, artificial epilepsy and sectioning the spinal cord, but most of the work that now appeared under his name on these subjects was little more than a revamping of his former work His lectures were faithfully recorded in the *Lancet*, and those delivered in 1859 were printed in Philadelphia as early series had been The content of the slim volume was entirely clinical, as its title suggests, *Lectures on the Diagnosis and Treatment of the Principal Forms of Paralysis of the Lower Extremi-*

ties[17] It was successful enough to be translated into French and to pass through two English editions Nevertheless, Brown-Séquard's original work after the almost feverish productivity of his first ten years was now diminished to a thin trickle, and he was content to pad his bibliography with case histories, such as his account of a Mr Fillmore, captain of a sailing vessel, who was stabbed in the neck while in the harbor of lawless San Francisco in the Gold Rush period, and who when examined eight years later showed the typical Brown-Séquard syndrome[18]

His interest in body temperature, which had earlier been so ably shown in his experiments on stimulating the cervical sympathetic nerve, reappeared in two articles in his *Journal* He found that plunging one hand into cold water lowered the temperature of the other[19] He also announced the observation that the effect of tropical heat is to raise the mean temperature of the human body, but the increase is usually less than one degree[20]

His work on the respiratory center reported in 1858 and 1860[21] has found its way into almost every modern comprehensive text-book of physiology, only for it to be pointed out that his idea was a mistaken one and that the evidence which he brought forward

chest, resembling normal respiratory movements, occurred after each stoppage of the artificial respiration, provided the period of asphyxia was not too prolonged

The later references of others [24] to this work would have us believe that Brown-Séquard had actually "described respiratory centers in the cord" In none of his own papers is he quite so specific The nearest he came to claiming the existence of subsidiary respiratory centers outside the medulla is his statement in one of his lectures before the Royal College of Surgeons in London [25] to this effect, "All the facts mentioned, and many others of which I have no time to speak, have led me, first, to abandon the view so generally admitted, that the medulla oblongata is the essential source of the respiratory movements in the nervous centers, and secondly, to propose the view that these movements depend upon all the *incito-motory* parts of the cerebro-spinal axis, and on the gray matter which connects those parts with the motor nerves going to the respiratory muscles" In all his experiments the movements he observed could have been nothing more than those produced in the early stages of asphyxia The final cessation of respiratory movements after removal of

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the medulla and the *nocud rud* he attributed not to the loss of this region of the nervous system, but to inhibitory impulses coming from neighboring nervous centers, chiefly the vagus center, whose inhibitory action on the heart had made such a profound impression on him in his early days His theory was stated thus " It is in part to the irritation one produces in removal of the medulla in its entirety or of its central parts (*nocud rud*) that is due the sudden suspension of respiration These experiments show that the physiology of the medulla as the respiratory center must be entirely revised " [20]

It is impossible not to be aware of some deterioration in the quality of his experimental work beginning in this period Hardly any of it from this time on was to resist the test of time As he grew older his prejudices and intuitions overrode his critical faculties His scientific reputation would actually have been better if he had stopped experimenting in 1856 Although many of his later ideas were startlingly new and along the right lines, he ceased (one would guess) to ask, " How will nature act under certain conditions? " He rather put the question, " What conditions can I set up so that I can demonstrate to others the way I think that nature will act? "

In much of his later work he seems to have decided that because of his experience in the laboratory and the clinic, he knew what ought to happen, and he then directed his experiments so as to show that his idea was correct, undisturbed if the data sometimes suggested conclusions other than those which he was prepared to draw from them His paramount object in these experiments on the respiratory center seems to have been to prove Flourens wrong, as he had earlier proved Bell and Longet wrong in regard to the pathway of sensory impulses in the spinal cord It is true that some years later two other investigators repeated and extended Brown-Séquard's experiments, and satisfied themselves that there were subsidiary respiratory centers in the cord, but the current physiological opinion is that Flourens' work stands, and movements of the chest after removal of the medulla are still considered products of an asphyxial condition

It was natural that many of his contemporaries should refuse to accept his conclusions regarding the *noeud vital*, and the attitude taken by his close associate, Vulpian, is characteristic At the time Brown-Séquard left the National Hospital for the Paralysed and Epileptics in London, Vulpian was

lecturing on the nervous system at the *Muséum d'histoire naturelle*. He cited his friend's early experiments on frogs and toads which lived for months without a *noeud vital* (these cold blooded animals had, of course, obtained sufficient oxygen through their moist skins to maintain life), and he repeated the joke which went the rounds after Brown-Séquard first reported these experiments, "The vital spot seems to be unnecessary to life." But when it was a matter of higher animals, i. e., birds and mammals, the lecturer could only conclude that death following destruction of the respiratory center was nothing more than the result of abolition of all respiration. Furthermore, he stated that he had never seen any spontaneous movements in such animals deprived of their *noeud vital* and kept alive by artificial respiration, although the cord was still active, as was shown by the fact that reflexes were easily provoked at the time of observation.

In these lectures Vulpian, in spite of his criticism of the work on the respiratory centers, had high praise for his friend's earlier work on the spinal cord. He said, "It is true that the physiology of the spinal cord has made notable progress in recent times, thanks above all to Brown-Séquard."[27] He pointed

out that before Brown-Séquard no one had shown crossing of the sensory elements in the cord, but he did take exception to the latter's view that what sensitivity the dorsal columns possessed was borrowed, as it were, from the dorsal roots of the spinal nerves Brown-Séquard had endeavored to explain the sensitivity which even he had not been able to deny to Bell's dorsal columns as being derived from some other part of the nervous system This was but another example of his principle of nervous "action at a distance," i e, that activity of almost any part of the nervous system could set off or restrain action in another part, so that no region of the brain (in particular) could be said to have a definite and invariable function, since its behaviour was dependent upon the action of some other, often distant, part The idea was not new with him, but had been in his thoughts for some ten years, and was eventually to color his entire concept of the function of the nervous system

4

The London Hospital for the Paralysed and Epileptics was now a closed chapter for Brown-Séquard,

and 1861 saw him once more in America. It was perhaps on the way to take the boat at Liverpool that the following incident occurred. He is said to have been offered a fee of two hundred pounds to go from London to Liverpool to examine a patient. He replied that he would stop over the next day on his way to New York and that the fee would be his usual one of five guineas. Another story to show his disregard for the emoluments of a successful consultant probably belongs to a rather later period. Once when he was in Le Havre (where he spent a number of summers during the 1880's) he was asked by an American to go to Italy to examine the man's son, who was ill there. A few questions put to the father showed that the case was not exactly in Brown-Sequard's special field of practice. He therefore refused to take it and recommended another physician. The father was insistent and offered a fee of fifty thousand dollars, but Brown-Sequard refused to alter his decision. Money was never a first consideration with him, and it was with no regret, but rather with relief, that he abandoned his lucrative practice in London, as he had done earlier in Paris.

Hardly had he landed in the United States when another professorship was offered him. On June 11,

1864, in spite of the continuance of the Civil War, the Corporation of Harvard Medical School voted to establish a Professorship of the Physiology and Pathology of the Nervous System Perhaps the reason for their being willing to set up this new chair in such difficult times and to give the appointment to Brown-Séquard is to be found in the following stipulation "The compensation of the Professor is to be derived from fees," this being the usual manner of compensation for the medical schools at that time He accepted the appointment, and the *Boston Medical and Surgical Journal* announced with confidence that the new professor had now "fixed his residence permanently among us" How little they knew their new professor! He did take a house in Cambridge, and formed there one of his strongest friendships, with Louis Agassiz (1807-1873), the celebrated Swiss naturalist, who had brought such fame to Harvard College

Brown-Séquard duly began his lectures on the nervous system at Harvard Medical School in January, 1865, but he presently decided that his health was not equal to finishing the course It is with no surprise by this time that we find him on February 3 across the Atlantic in Dublin, where there was

great excitement in medical circles over the excision, under the Harvard professor's advice, of a vertebra in a patient whose spine had been injured in an accident

A lecture which he gave in Dublin marks the crystallization of the attitude he had taken regarding the place of physiology as a science It bore the title, " On the importance of the application of physiology to the practice of medicine and surgery " The telling point of his lecture was the claim that before he began his experiments demonstrating the crossing of sensory pathways in the spinal cord, no one could understand such cases of human hemiplegia as had just been shown him in the Dublin hospitals He cited in illustration an incident occurring after the delivery of one of his lectures in London under the auspices of the Royal College of Surgeons He said " That eminent Physician, Dr T Addison (whose modesty, like that of all truly great men, was in proportion to his great talents and extensive learning), did me the honor of asking me about a case in which there was (1) coldness in one half the body, (2) tingling of the fingers, (3) ptosis in the right rectus muscle and (4) jerks in the muscles of the face on the side opposite to the injury This in the human species

was new to me, but from my animal experiments I said it was a case of disease of the *pons Varolii*—as it proved to be" The concluding sentence was, "Physiology ought to be more studied than it is"

On October 5, the Faculty of Harvard reported receiving by the latest steamer a letter from the missing professor He was in London and wrote that after packing his furniture and engaging his passage for America he had been attacked by an old malady and was unable to do active mental work his lectures would not be given that winter

According to the account of M Eugène Curé, a Mauritian friend, he and the Brown-Séquards were living at this time at the house of Dr Victor Bazire in Bloomsbury, not far from the British Museum Brown-Séquard was evidently carrying on some experiments with guinea pigs once more, since M Curé, who was at that time a student in pharmacy, used to accompany the professor to Tottenham Court Road to purchase and carry home a supply of these animals A sidelight on Brown-Séquard's manner of life is cast by M Curé's anecdote that he on certain occasions abandoned his studies for an evening and succumbed to an invitation to attend one of the performances at Covent Garden, where Mrs Bazire's

father was conductor of the orchestra He felt that he should conceal such frivolity from Brown Séquard, who believed that a student should spend all his time at his studies, as he himself had done in his youth On his return from the opera, M Curé would dismiss his cab at some distance from the house and enter by stealth On one occasion he was detected and at lunch next day Brown-Séquard reproved the young man for his lapse from duty Perhaps if the earnest scientist had himself taken a night or two off occasionally to go to an opera, he might have kept his nerves under better control and needed less often to take flight from difficult situations and try to recover his poise on an ocean voyage There is testimony that his excessive zeal for work would often lead him to spend as much as twenty hours a day on his experiments He never went to the theatre or to a concert It is even said that he never took a walk for pleasure He actually hated spending valuable time on anything but his work

Communion with the guinea pigs had a restorative effect, and in April, 1866, he was back in New York In November he resumed his lectures in Boston They were attended by a large class of students and physicians, and we can assume that the harvest of

fees was satisfactory He was chosen, moreover, to give the opening lecture of the winter term, on November 7, 1866, to welcome the incoming class of medical students This lecture has been preserved, since it was, as its title page informs us, " printed for the class " The advice he gave was characteristic, and sound enough To learn, students must themselves work He recommended the method approved by the medical students of Paris the formation of small groups of three or four meeting daily, each member " being prepared to deliver a short lecture to the others on a freshly studied subject " Next, he confessed that he could not understand how anyone could have a clear idea of physiological processes without practical demonstration He therefore advised students to procure frogs and rabbits for a " small number of well-devised experiments made by yourselves " Although he agreed with the motives of the societies for the protection of animals, he did " radically dissent from them in the attempts they have made in Europe and here to check, if not prevent altogether, certain works of scientific research, the great object of which is the good of mankind " He outlined the syndrome known by his name, reported the startling movements of a " much

beloved patient who had died of cholera, whose arms during the onset of *rigor mortis* rose at right angles to the trunk, the hands advancing toward each other so that the fingers of one side came to cross those of the other side, as is done by Catholics in prayer. The sight of the importance of knowledge of positions, he urged the students to try original investigation for themselves. Toward the end of his address he indulged in frankness which must have been a severe test of the reverence in which the foreign professor was held by the Harvard students of that day. He said

But, I am asked how can we learn to make scientific or practical investigations in physiology or medicine in a country like this where the teaching of these sciences is not only rudimentary? I do not deny that there is a great need here of an institute, where the means of prosecuting scientific researches should be taught by competent men. I have no doubt that he who would establish such an institute would be a benefactor of the human race, not only in this Republic, but all over the world, while he would also do much at the same time, to place this country on a level with Europe, for things about which the inferiority of America is notorious.*

These words are at the same time an ominous prophecy that Brown-Séquard could never be happy

at Harvard He was in exile as a scientist The bitterness of the exile seems to color another passage in the address in a significant way

Let me repeat [he said] that it is not so difficult as you may imagine to make discoveries in the medical sciences Without any wish of diminishing the merit of one of the most ingenious discoverers in physiology in our time, I will point out to you how easily he made the discovery of the important fact, that, in certain circumstances, the liver is gorged with sugar One day he decided that he would test for sugar every organ in the body, and in a very short time, and with very little labor, he ascertained that, except the liver, there is either no sugar, or only an extremely small quantity of it, in all the organs of the body This being discovered, he examined the portal blood near the liver, and found that it contains no sugar, while, on the contrary, in testing the blood coming out of the liver, he found it very rich in sugar Hence the theory,—now proved false, but which nevertheless has been most useful to science in opening a new field,—that it is a function of the liver to make sugar

In spite of the disclaimer at the beginning, could any account of the circumstances of one of the most striking and significant discoveries in nineteenth century physiology be more devastating in its effect than this one of the work of his rival, Claude Ber-

nard? The phrases, " a very short time," " very little labor," stand for some ten years of unremitting effort to complete the story of glycogen in the liver, and then, at the very end, the last step was anticipated, and another investigator was the first actually to isolate the critical substance, just as Brown-Séquard had anticipated Bernard in providing the final proof of the existence of vasomotor nerves The struggle between a natural generosity and resentment (probably unacknowledged) over Bernard's secure place in the scientific world of Paris may be invoked to explain the belittlement introduced obliquely here

Boston, in spite of its pride in being the intellectual center of the New World, was certainly not the place for Brown-Séquard His friend Agassiz realized this, and urged him to go back to Paris on the ground that it was the best place for him to carry on his physiological studies To one who reads the catalogue of Harvard Medical School for the years 1867-1868, it might seem that there was on the part of this faculty an overwhelming interest in physiology, since nearly half of the professors appeared to be engaged in the pursuit of this science, Oliver Wendell Holmes (1809-1894) bore the title of Parkman Professor of Anatomy and Physiology,

Jeffries Wyman (1814-1874) was Professor of Comparative Anatomy and Physiology, and Brown-Séquard is down as Professor of Physiology and Pathology There was interest, but the times were not yet ripe The Harvard Medical School did not provide laboratories and materials for original research Agassiz, although he succeeded in having the brick and iron barracks of a Museum built on Oxford Street in Cambridge, maintained in summer his own private laboratory on the Massachusetts coast at Nahant The general idea that research and original investigation were adjuncts to a professorial post had not yet invaded the American academic world Agassiz wrote the strongest recommendations to Paris urging the Minister of Education to do something for his friend In return for these favors Brown-Séquard was happy to serve as Agassiz's physician, the health of the famous zoologist having broken down at this time The physician's chief prescription was, "No tobacco!" This was a great privation to the patient, who was very fond of his cigar On his return to Boston in 1866 Brown-Séquard had been interviewed by the *Philadelphia Medical and Surgical Reporter* (August 25) and was asked his opinion on smoking "I never smoke,"

was the reply, "and have seen the most evident proofs of the nefarious effects of tobacco on the nervous system" An almost fanatical proscription against the weed was a regular feature of his treatment

He was, however, loath to engage in general practice, and a notice appeared in the *Boston Medical and Surgical Journal* for January 10, 1867, to the effect that although Dr Brown-Séquard had consented, when he came to Boston, to see patients twice a week at the city office of Dr George C Shattuck (1813-1893), Dean of Harvard Medical School, he had now decided to give up altogether the practice of medicine He made an exception only in the case of his special friends

Agassiz, as one of America's foremost scientists, had great influence in two of the New World's scientific societies, the American Academy of Arts and Sciences, founded by John Adams in 1770 as a Bostonian rival of Benjamin Franklin's Philosophical Society at Philadelphia, and the National Academy of Sciences recently (in 1863) created at Washington to give advice to the Federal Government on scientific matters Agassiz had actually been one of the fifty incorporators of the National Academy, and its

roster included the names of many, if not the majority, of the most active and eminent scientific investigators of the country [29] The Bostonian society was the first to recognize Brown-Séquard, electing him Fellow, May 28, 1867 Later, in 1873, after he had left Boston, his status was changed to Associate Fellowship, and finally in 1881 to Foreign Honorary Membership The Washington society promptly followed the lead of Boston, and made him Fellow in January, 1868 His father's native country had done its best to honor its foster child

But Brown-Séquard could not really take root in the United States The death of his wife at the end of 1867 was enough to make him give up his Harvard professorship altogether and to send him back to Paris by way of Dublin with his twelve-year-old son in the spring of 1868 An additional honor had come to him early in this year in his election to the Paris Academy of Medicine Because he gave his general address as New York, he was made "foreign corresponding member," and although later on he made Paris his headquarters for many years, he remained "foreign corresponding member" until his death

When he arrived in Paris he began another journal,

Archives de Physiologie normale et pathologique, with the assistance of two of the most celebrated specialists on the nervous system in Paris, if not in the world, Charcot (1825-1893) and Vulpian. The title of this new journal is similar to that of the one founded by his old friend Charles Robin in 1861, *Journal de l'Anatomie et de Physiologie normales et pathologiques de l'homme et des animaux*, when Brown-Séquard ceased to publish his *Journal*. The choice of title for Robin's *Journal* was doubtless influenced by the fact that it was actually founded under the joint editorship of the two friends, but because Brown-Séquard could not agree to Robin's policies, he withdrew after the fifth number, leaving Robin the sole editor. There was evidently enough material to supply both Robin's *Journal* and Brown-Sequard's *Archives*, for both continued to appear concurrently until some time after the death of their founders. The new *Archives de physiologie* was frankly on the "applied" side, and the introduction to the first issue stressed the value to medicine of experimental physiology in the past twenty years, as well as the help that physiology on its side had received from the clinic. Furthermore, since it was a recognized fact that the dividing line between physi-

ology and pathology cannot be sharply fixed, the editor of the *Archives* reported himself ready to accept papers on both subjects

It may seem strange to us now that Vulpian in his lectures of 1864 ridiculed the idea which had recently been put forward by Schiff that there could be separate fibers for touch, pain, taste, colors, and the like, but he did so Just as his lectures were going to press four years later Vulpian read the article which Brown-Séquard proposed to publish in the first volume of the new *Archives* Here Brown-Séquard maintained that in the spinal cord conductors for touch, tickle, pain and temperature were separate from each other, that each of these different senses occupied a distinct part of the cord, that in the upper part of the cord the conductors from the lower limbs and muscles of the trunk lagged behind conductors from the arms and neck, and that all these conductors cross in the cord while conductors serving muscles do not The actual observations had been made in 1865 and were now summarized in this article to be published three years later [80] Although the arguments set forth in this manuscript convinced Vulpian that he was wrong in ridiculing the idea, he did not wish to alter the text of his lectures They

were finally printed in the form in which he had delivered them, but he indicated in a foot-note his change of heart and his thorough agreement with his associate editor on this point Brown Séquard was much happier in his conclusions on the physiology of the tracts in the spinal cord than in those on the *nocud .ital*

He had the habit of recording every possible bit of data from his own experiments, as well as chance observations on his patients or himself These notes were written on odd scraps of paper, old envelopes, wrappings in which his scientific journals had come, any piece of paper which came to hand, this frugality having survived from a time when money even for writing paper was hard to come by The closets of whatever residence he happened to be occupying were crammed with boxes of such notes As an instance of the uses to which he put these meticulous, although random, observations, we may cite the "Personal observations on whitening of hair suddenly," which he published in the second volume of his *Archives* in 1869 The article has reference to jottings made in August, 1862, when he was in London His beard at this time was black in front, but sprinkled with white near his temples and ears

He woke one morning to find white hairs in front where none had been before He removed them, five on one side, seven on the other Two days later two more appeared on the left, three on the right, and they were white through the entire length of the whisker from root to tip He at once removed these offenders and repeated his observations over a period of 5 to 6 weeks White hairs always appeared overnight He concluded that it was quite possible for hair to become white in the course of a single night [31] Many of his later papers are based on similar observations made years before So carefully had the notes been taken that the date and circumstances attending each observation are always recorded in the published communication

While he was in Paris he attended meetings of the Academy of Medicine to which he had so recently been elected The subject of his communications here was epilepsy Certain of his colleagues refused to see the parallel which he invariably stressed between symptoms displayed by his "artificially epileptic" guinea pigs and human epileptics, even although he reported that when more than ten years before he had given a demonstration to the members of the Academy in their library, all those present,

including the celebrated Cruveilhier (1791-1874), had professed to be profoundly impressed and thoroughly convinced

He was still without settled prospects when a young graduate of Harvard, Henry P Bowditch (1840-1911), came across the Atlantic to work with him The American had come to Paris at the urging of Dr Jeffries Wyman, a good friend of Brown-Séquard in Boston, under whom Bowditch had studied comparative anatomy at the Lawrence Scientific School of Harvard He had also been a student at Harvard Medical School in 1866-67 during Brown Séquard's professorship Unfortunately Brown Séquard could offer the young man no place to work in Paris, but he sent him to attend courses by Bernard and Ranvier (1835-1922) Bowditch, however, got his real push in the direction of experimental physiology from Ludwig (1816-1895) in Leipzig, and when he returned to Harvard Medical School in 1871, bringing with him German-made apparatus of Ludwig's design, he managed to persuade the authorities to allot him two attic rooms in the old medical buildings on Grove Street, Boston, for the installation of the new equipment Thus the advice given by Brown-Séquard to the entering class

of Harvard Medical School in 1866 could now be put into practice, and the first physiological laboratory for the use of students in the United States was established at Harvard, not by Brown-Séquard who had pointed out the need for it, but by one of Harvard's own sons, Henry P Bowditch

5

In February, 1869, a Boston medical journal[82] reported that it had received information from a reliable private source that Brown-Séquard had been offered a chair on the Paris Faculty of Medicine, and that the French Government had decided to build a laboratory for him near the Medical School in the garden of the *Hôpital des Cliniques* His American friends were delighted that recognition was coming at last, but unfortunately reality did not quite come up to this anticipation of it The truth of the matter was that in the perennial shuffling of professorships in Paris, the creation of a vacancy had, as usual, given rise to exaggerated rumors Just before Claude Bernard's laboratory was shifted from the Sorbonne to the *Muséum d'histoire naturelle,* it had been thought that Brown-Séquard was to be given the

chair in Comparative Physiology at the latter institution. Bernard proved to be too formidable a rival. He went to the *Muséum*, Paul Bert got the chair vacated at the Sorbonne, and Brown Séquard was again left with no appointment. Now, however, it appeared that after all he was to be honored with an appointment to the Chair of Comparative Medicine in the Faculty of Medicine, a chair which had been created for Rayer (although he had never given the lectures) and which since his death had been vacant. There was to be a change in the title, so that the chair would now be called the Professorship of Experimental and Comparative Pathology. He was not satisfied with nomination to the chair by the Minister of Education and refused to accept until the vote of the Faculty of Medicine had been declared in his favor in addition to the governmental nomination. In February, 1869, he did accept.[33] As he was still an alien, a British subject, he was not eligible for the actual professorship, but functioned as *chargé de cours*.

The course of lectures was well attended and his demonstrations in the amphitheatre to show the effects of lesions on the nervous system were especially popular, too much so for the budget of the

Faculty of Medicine Notice had to be sent out that Brown-Séquard's lectures, which were to have continued until the winter course began, would be cut short because the Faculty of Medicine refused to furnish the necessary material for the demonstrations His demand for animals, which he housed at the *École pratique*, had been greater than the budget would stand [34] Reports of the lectures which he did give showed that he had not tried to astonish his audience by flights of oratory, but had presented the results of his own investigations with a simplicity and sincerity so effective that his course was acknowledged on all sides to have been most successful

It was in the course of these lectures that, following up the suggestion contained in his work on the adrenals, he advanced the idea that internal secretions were useful, if not necessary, to the bodily economy He even proposed that if semen were injected into the blood of old men, they would probably show signs of renewed vigor As we shall see, it become the dominating motive of his later life to prove correct this idea of the possibility of restoring the powers of the aged by injection of testicular extracts

His other absorbing interest at this period was

still "artificial epilepsy," and he bore abundant witness to it in his contributions to the meetings of the *Société de biologie*, which he never failed to attend while he was in Paris.

He was not yet reconciled to a settled residence even in Paris, however, and when the war of 1870 began, he was actually on the way to New York, and he remained abroad for its duration. He gave lectures in America, the proceeds of which were sent to France for the benefit of wounded soldiers. It is reported that considerable sums were raised by his efforts. On his return to Paris in 1872 he resigned his appointment in the Faculty of Medicine in favor of his friend Vulpian, and Vulpian's chair went to Charcot. The reason for this rearrangement was apparent, when, on his return to New York, he made his second marriage, again to an American woman, Miss Mary R. Carlisle of Cincinnati. It was evidently his plan to establish himself in practice in New York. That he really meant to remain in America is indicated by his starting the publication of another journal there, while maintaining his editorship of the *Archives*, which still flourished in Paris.

The new journal was in English and was called

Archives of Scientific and Practical Medicine—the word "physiology" did not appear even in a subtitle His co-editor was Dr Edward Constant Seguin [35] (1843-1898), who after taking his medical degree in the United States had gone to Paris in the winter of 1869-70 to work with Brown-Séquard and Charcot, specializing as one would expect, on diseases of the nervous system There was a further bond between the two editors of the new *Archives* in their common interest in the subject of body temperature It has already been noted that Brown-Séquard had published several articles on this topic, and to Dr Seguin is due the credit for the introduction of the thermometer into American medicine, an instrument which is now at least as characteristic of the medical practitioner as the stethoscope The appearance in the *Chicago Medical Journal* of 1866 of Seguin's paper on the use of the thermometer is said to have marked the real beginning of American medical thermometry It was only natural that when Brown-Séquard returned to New York with the evident intention of residing there permanently he should have joined forces with this former pupil of French extraction, whose interests were so close to his own Also in New York and in charge of the small labora-

tory where on Saturdays experimental work was carried on, was Dr Eugene Dupuy (1847-1921), another pupil and a fellow countryman in the strict sense, since his father had been one of the Mauritian students resident in Mme Brown's pension in 1840. This was the beginning of an association that lasted Brown-Séquard's lifetime.

The *Archives of Scientific and Practical Medicine* proved to be very shortlived indeed. The numbers appeared monthly, beginning in January, 1873, through five issues—a single article constituting the June and last issue. The fugitive journal is chiefly remarkable because in it is to be found the editor's first memoir on his idea of "inhibition," that property of the nervous system by which a restraining effect is transmitted from one part to another. There is also a personal reference in one of the issues which may be worth recording. To the account of his own dyspeptic condition of twenty years before he appended these words: 'Since that time up to this moment, his (i.e., Brown Séquard's) life has been one of great hardship, which he has borne remarkably well." One is inclined to punctuate this sentence with an exclamation point, although there is none in the original. It was true that he was having

an especially hard time at the moment of writing, for he afterwards said that the 1870's were the worst years of his whole life

As usual in a crisis he crossed the Atlantic, and July of 1873 found him utterly miserable in England's center for invalids, Brighton He was almost desperate Not only was he himself ill, but he was seriously worried over the health of his wife Nevertheless, he was back again in New York in three months' time after the short futile attempt to better their condition at the Channel health resort, and now it was a struggle for money Unlike his clients in Paris and London, his New York patients paid badly He wrote "Despair and incertainty, these are my lot"

Agassiz tried to help During the previous summer he had held the first session of his biological laboratory on Penekese Island in Buzzard's Bay, a project which had been made possible through a generous gift of fifty thousand dollars from the wealthy New York merchant, Mr John Anderson Agassiz proposed that a chair of physiology be established at his laboratory during the next summer session for his friend, and he promised to solicit funds from his patron for such a chair Unhappily, Agassiz died

December 14, 1873, and his death put an end to the plan. Contrary to Brown-Séquard's advice, Agassiz had smoked several cigars on the occasion of a family dinner early in the month, and the next day was attacked by dimness of vision and paralysis of the larynx. Brown-Séquard was in New York at the time. He was sent for and arrived to attend his friend. He and another physician, Dr. Morrill Wyman (1812-1903), were present when the naturalist died, and also at the autopsy, where it was found that Agassiz's brain was very large and heavy, like that of the famous French naturalist, Cuvier (1769-1832).[6]

During 1874 Brown-Séquard's second wife died after only two years of marriage, and he was left with an infant daughter, born in that year, to be taken care of. The child was named Charlotte for her paternal grandmother.[7] He seems to have been unhappy, too, over his son, now eighteen years old, who somehow failed to fulfill his father's expectations. There is a glimpse of the two together in a reference made by Brown-Séquard to his son helping to hold guinea pigs, while his father applied the cautery as a stimulus in an experiment on the brain. At this time Brown-Séquard was quite undecided as

to where he should try to live He lectured in Boston during 1874 at the Lowell Institute on "nervous force," and during 1875 in New York on blindness and hemiaesthesia, in Boston again on the localization of function in the brain, in Dublin on anaesthesia, amaurosis and aphasia caused by lesions in the brain, in London at the Royal College of Physicians on the pathological physiology of the brain He was back in Boston in the summer of 1875, and Agassiz's family allowed him to use the small private laboratory at their summer cottage at Nahant for some experimental work Nearly fifteen years were to elapse before he told of the experiments he did that year at the sea shore [38] His idea of rejuvenation of the aged was being submitted to the test Into a dozen old dogs he attempted to graft whole testes of young guinea pigs, or fragments of these glands He was successful in only one case, but this one success so encouraged him that he was finally led to perform related experiments on a human subject, with such dramatic results that the medical world was stirred to its foundations

Throughout this period of indecision, while he was shifting about from place to place, he was everywhere crusading strongly against the new doctrines

of localization of function in the cerebral cortex which were revolutionizing the science of neurology. Before 1870 it was universally held that the cerebral cortex acted as a whole, that it could not be excited by artificial means, and that lesions in it resulted in no specific defect, but only in a generalized depression of nervous functions. This was the consequence of Flourens' early excellent work on the pigeon's brain. The bird had been unfortunate experimental material to choose, if one thought, as experimenters at first did, that conclusions reached on this animal could be applied to the higher mammals, including man. In no other vertebrate structure are species differences in function more striking than in the cerebral hemispheres. This fact was only being realized in the 1860's. It is true that phrenologists somewhat earlier had tried to introduce the idea of localization of different functions in different parts of the human brain, but their unscientific nonsense had made little impression on physiologists. Broca had made the first real contribution in 1861 when he correlated aphasia in man with a lesion in the left cerebral cortex, in an area now known by his name, Broca's area. Hughlings Jackson had observed the same phenomenon, but was too late in recording

his observation to receive the credit for the discovery However, he did add a very pertinent point, in *left*-handed persons the lesion was to be found in the *right* cerebral cortex Then the whole conception of the functions of the mammalian cerebral cortex was changed almost over night by the classic paper of Fritsch (1838-1897) and Hitzig (1838-1907) in 1870, which showed that in the dog, at least, definite movements on one side of the body could be elicited by artificial stimulation of certain areas of the cerebral cortex on the opposite side, and that prolonged stimulation of this area led to general epileptiform seizures [89] This was squarely in Brown-Séquard's field, but he had been so impressed by the experiments on vagal inhibition which he had carried out in his younger days in order to prove that the Weber brothers' idea on inhibition were right and Longet's wrong, and he believed so strongly in his theory of nervous action at a distance, that he was blind to the significance of all this new work David Ferrier (1843-1928), who at once took up the systematic exploration of the excitability of the brain, said in his Croonian lectures, delivered before the Royal College of Physicians in 1890, "The difficulty of discriminating between the direct and indirect effects

of cerebral lesions has furnished Brown-Séquard with arguments for his peculiar views that symptoms of cerebral disease are due to some dynamic influence exercised by the lesion on parts situated at a distance (and always apparently out of reach) which are credited with the functions lost or otherwise disturbed" So late as 1890 Brown-Séquard still maintained that the results of electrical exploration were of no greater significance than the contortions induced by tickling the sole of the foot,[40] but, as Ferrier correctly retorted, from these very results had been developed the whole modern doctrine of cerebral localization

Brown-Séquard first began to be emphatic in his denunciation of the doctrine in his short-lived *Archives of Scientific and Practical Medicine* The immediate occasion was his attempt to prove Wallaston (1766-1828) wrong in his contention that only part of the optic nerve fibers from the retina of each eye cross in the optic chiasma of man According to Wallaston's theory, destruction of one optic tract central to the chiasma should not cause complete blindness in a single eye, but should result in partial blindness of both eyes Brown-Séquard's argument against the theory was that when his pupil, Eugene

Dupuy, using guinea pigs for the experiment, sectioned the chiasma in the median line, or sectioned one optic tract, instead of hemiopsia of both eyes, one eye was found to be completely blind From this experiment on the guinea pig he concluded, "Amaurosis in cases of lesion of either one optic tract, or the tuber quadrigeminum, or other parts of the encephalon, or one side of the spinal cord, are not due to loss of function of conductors of visual impressions or a part of the center of these impressions, but to an influence in the nutrition of the eye, of the optic nerve or other parts by an irritation starting from the site of lesion"

This is a perfect example of Brown-Séquard's use of data taken from correct observations to try to prove a proposition which was incorrect Wallaston was perfectly right in his theory, and Dupuy's observations were correct The reason for Brown-Séquard's conclusion being false is that the arrangement of optic nerve fibers is not the same in man as in the guinea pig In the lower mammals there is virtually complete crossing of fibers in the chiasma, in man, fibers from the temporal side of the retina do not cross, those from the nasal side do It was uncritical insistence upon applying guinea pig

anatomy and physiology to the human being which led him into error, but once having committed himself he seems to have carried his conclusions further than was reasonable, and, moreover, we cannot let pass unchallenged his statement that lesion of the spinal cord produces amaurosis

Amaurosis, according to any modern dictionary, is "a loss or decay of sight from loss of power in the optic nerve, without any perceptible external change in the eye" Brown-Séquard's recent papers on this subject up to 1873 [41] had merely reiterated the statement which he had often made that lesions in the spinal cord, restiform body, or cerebellum led to amaurosis, and that the defect "depends on an influence exercised at a distance altering the nutrition, either of the retina or some other part of the nervous visual system" A careful survey through his earlier papers to discover the experimental basis for this view leads us back to 1850, when he described the retinal disturbances in the eye attendant on hemisection of the cord Here he says, "Everyone knows that the existence of helminthes in the intestinal canal, as well as certain diseases of the spinal cord, can lead to troubles in vision or even diseases of the eye, and sometimes complete amaurosis" [42]

Now, the troubles he found were inflammation of the conjunctiva, corneal opacities, corneal ulcers, opacity of the lens, and finally, in late stages, utter breakdown of the tissues composing the globe, so that the eye was entirely emptied of its contents Loss of sight under these circumstances would be a secondary effect, and would not be, strictly speaking, amaurosis We therefore gain an erroneous impression when he says, "Hemisection of the cord leads to amaurosis," because this implies that the loss of sight which may sometimes follow the operation is strictly comparable to that which immediately and irrevocably follows from injury to the retina, the optic nerve, or the optic tract He must have thought of amaurosis as loss of sight from any cause whatever, and this would explain his association of the results of Dupuy's experiment where the loss of sight was true amaurosis because of interruption of the appropriate nerve tracts, with the malnutrition of the eye and interference with sight frequently occurring in his guinea pigs after lesions in the cord

When he was asked to give the Smithsonian Institute's Toner Lecture in Washington in 1874 he chose as his subject, "The dual character of the brain" [43] In this lecture he insisted again that "an

alteration in any part of the nervous system, whether in the brain or elsewhere, can, by producing an irritation, act on other parts, so as to produce the loss of a function of those other parts, and so it is especially with sight In many experiments I have ascertained that injuring a small part of the spinal cord produces a loss of sight in the eye on the same side An injury to the *medulla oblongata*, a little higher than the part of the spinal cord which produces loss of sight on the same side, will produce a loss of sight, but in the opposite eye There is, therefore, a power of producing a loss of sight by irritation, and indeed there is nothing more common in children having worms than a diminution in the power of seeing" This again shows the confusion into which he had fallen His nerve cutting might impair the nutrition of the eye, and this in turn might lead to blindness, but it is unbelievable that cutting the cord would have as its immediate consequence loss of sight, while the connection between worms and amaurosis is still more baffling

Two years later, in his lecture in Boston, "On Localization of Functions in the Brain," he admitted that Fritsch and Hitzig "are warmly supported by my eminent friend, Prof J Charcot of Paris," but he

held firmly to his own opinion, viz , " The character of symptoms in brain diseases is not in the least dependent on the seat of the lesion, so that a lesion of the same point may produce a great variety of symptoms, while on the other hand, the same symptoms may be due to the most various causes, various not only as regards the kind, but also the seat of the organic alteration "

His theories in this matter also influenced his treatment of human neurological cases, and he published in the *Lancet* a characteristically outspoken and fearless letter warning against surgery in brain disease If the localization theory were false and one could not tell the exact site of any disturbance of function in the central nervous system, surgery was not only futile, but, to use the expression he coined, " absolutely counterdicted " [44]

Charcot in the 1870's, as Brown-Séquard had remarked, vigorously upheld the localization theory, both in his lectures at the Faculty of Medicine and in his reports before the *Société de Biologie* The clash between the two friends was followed with the greatest interest in the Parisian medical world At one meeting of the *Société de Biologie* late in 1875 Brown-Séquard tried to corner the opposition

Charcot's version of the theory had been stated in these terms "The encephalon is not a homogeneous organ, but an association of diverse organs, each having distinct physiological properties, functions, etc" therefore, "lesions in certain regions will always produce the same symptoms" Brown-Séquard insisted that this was *not* the question, one should enquire rather, "Does destruction of certain regions of the brain lead to abolition of certain functions?" "Now that," he said, "is what I cannot admit" When he brought forward experiments on the dog to prove his point, Charcot, realizing the pitfalls in arguing from results obtained with the dog's brain to the human brain, refused to talk about the dog, because, he said, he had little knowledge of that animal The debate went on until Charcot finally refused to make further reply Whereupon Brown-Séquard said, "I regret that M Charcot withdraws from the discussion Science cannot make progress without criticism Nevertheless I shall continue to expose successively the different facts upon which my theory rests"—and he did so at length The trouble was that he had made up his mind, and no amount of evidence to the contrary could make him change it Charcot tried again and again to convince

him of his error, and the debate continued doggedly throughout the winter of 1875-6 These discussions led to Charcot's best-known publications, in which he showed that lesions in the so-called "silent areas" of the cerebral cortex caused no disturbance of motion whereas alteration in the motor area *always* produced on the opposite side of the body disturbances which might be paralytic or convulsive in nature (Jacksonian epilepsy in the latter case) He even found separate and distinct areas where lesions invariably led to disturbances limited to one limb or even to an isolated group of muscles From 1878 on, Brown-Séquard seems to have been almost the only neurologist of note who stubbornly refused to accept the localization theory

This clash with Charcot was evidently too much emotionally for Brown-Séquard, for he was off to America in 1877 He then received an invitation to become Professor of Physiology at Geneva and at once journeyed back to Europe and to Switzerland by way of London and Paris While waiting in Geneva before entering upon his professorship he married a third time His new wife was the English widow of the painter Doherty, née Elizabeth Emma Dakin For some reason which has not been made clear he

recommended graduates at the University of Geneva, he returned back to New York.

On February 10, 1878, Claude Bernard died. There was a vacancy to be filled in Paris for which Brown-Séquard's claims were unrivalled. He packed back to France to make application in person to the vacant Chair of Medicine at the *Collège de France*. His brother-in-law was to be his main support. On May 31, 1878, Maréchal de Mac-Mahon, Keeper of the Seal, President of the French Republic, signed the naturalization paper of Charles Brown (Charles Edouard), Doctor of Medicine, born April 8, 1817 at Port Louis on the Island of Mauritius, now living in Paris, to the enjoyment of the rights of a French citizen. On August 3 came the local for appointment as Professor of Medicine at the *Collège de France* as successor to Claude Bernard, deceased. He had finally at the age of sixty-one come home to France.

NOTES

LECTURE II

[1] Norwood, W F, *Medical Education in the United States before the Civil War,* Univ of Penn Press, Phila, 1944

[2] *Virginia Med & Surg Journ*, 3 174, 1854

[3] *Ibid*, 2 342, 1854

[4] Taylor, Wm H, Old days at the College, *The Old Dominion Journal of Medicine and Surgery,* 17 87-93, 1913 Dr Taylor was for many years Professor of Chemistry, Toxicology and Medical Jurisprudence at the Medical College of Virginia

[5] Ott, Isaac, *The Medical Bulletin,* 18 361 66, 1896

[6] Rayer, Charles, Recherches anatomico pathologiques sur les capsules surrénals, *L'Expérience,* 1837

[7] *C R. Acad d Sc*, 43 422, 542, 1856, *ibid*, 44 246, 1857, *Arch gén de méd*, 8 385, 572, 1856

[8] Dale, Sir Henry, Natural Chemical Stimulants, *Edin Med Journ*, N S (ivth), 45 461, 1938

[9] *Bull Acad de Méd*, 21 1067, 1856

[10] D Clapp, Boston, 1857 82 pp

[11] Penfield, W & Erickson, T C, *Epilepsy and Cerebral Localization,* Thomas, Springfield, Ill, 1941

[12] Brown, T Graham, Studies in the reflexes of guinea pigs I The scratch reflex in relation to Brown Séquard s epilepsy *Quart Journ Exper Physiol*, 2 243 275, 1909

[13] Lippincott, Philadelphia, 1860

[14] H J Feltus was a descendant of Brown Séquard s great uncle, Canon H Feltus of St Stephen s Church, New York, from whom a letter to Pierre Paul Séquard in Mauritius, dated May, 1816, has been preserved The Feltus family had connections with the Fourierist Society, to the Massachusetts branch of which Brown Séquard had introductions from the Society in Paris, when he first visited America, although he himself was never a member The

Fourierist Society formed what they called 'phalansteres' where the apostles" lived together and worked for the common good

[15] On May 3, 1860, the Council for Election to the fellowships in the Royal Society placed Brown Sequard on their recommended list, which included among other names less well known those of Joseph Lister, the surgeon, and Francis Galton, student of heredity The list was voted upon June 7th, and Brown Sequard after this date was proud to write after his name the letters F R S

[16] Holmes, T, *A System of Surgery, Theoretical and Practical, in Treatises by Various Authors* London, Parker, Son & Brown, 1862

[17] Collins, 705 Payne Street, Philadelphia, 1861

[18] *Lancet*, Aug 9, 1862, p 166

[19] *Journ de la physiol de l'homme*, 1 197, 1858

[20] *Ibid*, 2 549, 1859

[21] *Ibid*, 1 217, 1858, *ibid*, 3 153, 1860, *Physiology and Pathology of the System*, pp 187-192

[22] Olmsted, J M D, Historical note on the *Noeud Vital* or Respiratory Center, *Bull Hist Med*, 16 343, 1944

[23] *Physiology and Pathology of the Central Nervous System*, p 191

[24] Cf Starling s *Human Physiology*, 1933, p 936

[25] *Physiology and Pathology of the Central Nervous System*, p 192

[26] *Journ de la physiol de l'homme*, 3 157, 1860

[27] Vulpian, A, *Leçons sur la physiologie générale et comparée du système nerveux faites au Muséum d'histoire naturelle* Baillière, Paris, 1866, p 365

[28] Brown Séquard, Prof C E, M D, *Advice to Students An Address delivered at the Opening of the Medical Lectures of Harvard University*, Nov 7, 1866 John Wilson & Son, Cambridge, 1867, p 32

[29] Bates, R S, *Scientific Societies in the United States* John Wiley & Sons, N Y, 1945

[30] *Arch de Physiol norm et pathol*, 1 610, 1868

[31] *Ibid*, 2 442, 1869

[32] *Boston Med & Surg Journ*, 80 71, 1869

[33] *Brit Med Journ*, Jan 16, 1869, p 52

[34] *Boston Med & Surg Journ*, 80 444, 1869

[35] I have not been able to discover whether this physician was a connection of the Armand Seguin who assisted Lavoisier in his experiments on respiration, and who is pictured in Madame Lavoisier s famous drawing of her husband s laboratory in 1788, seated on the right side in the picture, gas mask on his face, breathing oxygen from a tank, while Lavoisier collects the expired air in a jar over a pneumatic trough

[36] Marcon, Jules, *Life, Letters and Works of Louis Agassiz* Macmillan, N Y, 1896, v 2, p 213

[37] Charlotte Brown Séquard, now Mrs Bolton McCausland, widow of an Anglo-Irish physician, is at present living in England, and has been most kind in making available to the writer, in so far as she could, the details of her father s later life

[38] *C R Soc de Biol*, 41 415, 1889

[39] *Arch f Anat, Physiol u wissensch Med*, 37 300, 1870

[40] *Arch de Physiol norm et pathol*, 5° Sér, 2 199, 1890

[41] Cf *C R Soc de Biol*, 23 125, 1871

[42] *Ibid*, 2 134, 1850

[43] *Smithsonian Miscellaneous Collections*, Washington, 1877 (no 291)

[44] *Lancet*, July 14, 1877

LECTURE III

IN THE CHAIR OF MEDICINE AT THE COLLÈGE DE FRANCE

1

THE story of Brown-Séquard's professorship at the *Collège de France*, his scientific apotheosis, is inseparably bound up with that of his choice of an assistant, for although Brown-Séquard controlled the direction of the researches, it was d'Arsonval (1851-1940) who kept them going with his flair for mechanical devices The day to day story of the sixteen years can be gleaned from d'Arsonval's published correspondence [1] He was twenty-seven when Brown-Séquard succeeded to the chair, and he had been head of the physiological laboratory and Bernard's assistant at the time of the latter's death When Brown-Séquard began to plan for his first course of lectures, which was to begin December 2, 1878, he wrote more than two months in advance to d'Arsonval,who was at Limousin in the country-house where both he and his father had been born, to come to Paris to help make preparations The first series of

lectures and demonstrations (which were on the nervous system) went off well, but towards the end of the winter course of 1879-80, when the subject was the circulatory system, d'Arsonval in the midst of an experiment protested to the new professor, "Claude Bernard did not operate like this, Claude Bernard thought differently" Brown-Séquard was annoyed, words passed, and the upshot was that d'Arsonval and the aged laboratory servant, *le père* Lesage, who had held his post from the time of Magendie, together walked out of the laboratory Reconciliation was not too long delayed (although d'Arsonval withdrew briefly to Marey's (1830-1904) laboratory across a small courtyard), and when Brown-Séquard invited d'Arsonval to return as his substitute[2] it was with the injunction, "Treat me as you would treat Bernard " From this moment until the end of the association there was not only harmony, but a most affectionate relationship between the professor and his assistant

D'Arsonval's cleverness in planning electrical devices was brought into play from the very first Brown-Séquard, stung by Charcot's refusal to see the light regarding cerebral localization as he saw it, began his own experiments on stimulating different

parts of the nervous system When he galvanized (*sic*) the base of the brain he obtained movements sometimes on the same side of the body as the application of the stimulus, sometimes on the other [3] If, however, he stimulated the motor area of the cerebral cortex, he saw, as had Fritsch and Hitzig, movements on the opposite side of the body He thought the two cerebral areas must have mutual connections through the *corpus callosum*, since stimulation here affected both sides of the body simultaneously In a second experiment he claimed that when he cut the sciatic nerve there was loss of excitability to the galvanic (*sic*) current at the base of the brain on the opposite side of the body [4] The results of these two experiments furnished him with further examples of "inhibition" and "action at a distance," which was, of course, what he was really looking for Of these observations only that on stimulation of the *corpus callosum* has been preserved in present day physiological literature

"Inhibition" now having been demonstrated to his satisfaction, he turned to the exactly opposite property of "augmentation," which had been foreshadowed in his work as far back as his thesis of 1849 Some eight months' work was necessary before

the report was given toward the end of 1879 The example he presented before the Academy of Sciences was this if he sectioned by a transverse cut one lateral half of the base of the brain, this was followed by augmentation of motor properties in front of the cut, and by inhibition on the opposite side, in other words, in the first case a weaker stimulus than normal was effective, in the second, a stronger stimulus than normal was necessary to produce an effect [5] Both conceptions, "augmentation" and "inhibition," fitted in beautifully with his idea of action at a distance, not only could irritation in a nerve center dampen action at one distant center, but it could increase action at another [6] He soon introduced another method of producing nerve irritation besides cutting, viz , application of chloroform to the skin This seemed to serve his purpose just as well, for it gave the same results and simplified the operation [7] Finally, d'Arsonval invented a new method for nerve stimulation, condenser discharge, a refinement which today is considered more nearly to simulate the natural stimulus than the older galvanic or faradic current In this one respect, at least, solid progress was made

Brown-Séquard was struggling with a difficult

problem, which when finally taken over by Sir Charles Sherrington (1857 ——) and passed on to his pupils, became somewhat less vague and intangible than it had been throughout the preceding half century, although its expositors were still baffled in their attempts to make everything clear to the laity. Brown Séquard was, of course, fundamentally right, for the nervous system does act as a whole in that it has so many interconnections that influence of one part on another is strong. As Sherrington pointed out, any reflex act, even if local in its effect, is, in his own words, "a reaction to all sensificient stimuli incident on the individual at that moment in *sum* both as to space and as to time." It certainly does seem true that the discharge of even a single nerve cell can at one and the same time set one group of inactive cells into action and put another group of previously acting cells out of action. This is the well-known principle, often called "Sherrington's Law," of "reciprocal innervation of antagonistic muscles."

The observations on which Brown Séquard relied so heavily, viz., the heightening of the activity of the spinal cord after ablation of the brain, a phenomenon which is now known by the name which Sherrington applied to it, "facilitation," were not first made by

him E Weber in 1846, after his discovery of inhibition of the heart on stimulation of the vagus nerve, had explained " facilitation," which was known even before him, on the assumption that the increased activity was due to removal of an inhibitory influence of the higher centers Brown-Séquard at the beginning of his career, as has been pointed out, was much impressed by the discovery of the Weber brothers, so that he was acquainted with the explanation which they gave of the phenomenon of facilitation, but he had another suggestion which he first put forward in 1855 [9] He thought that nervous energy reflexly set free in the central nervous system could be divided into two parts, that which was liberated in the brain and that which was liberated in the spinal cord If liberation in the brain were impossible, all the force must go into the cord, hence the augmentation of reflexes on stimulating the cord after its being severed from the brain Although ingenious, this theory had no experimental backing, and therefore really nothing to recommend it His explanation clearly showed that Brown-Séquard did not think of nervous action in terms of nervous impulses passing over definite nerve fibers That he was actually hostile to this concept, which is the basis of

our present day ideas regarding the way in which the nervous system functions, is indicated by his violent rejection of the theory of cerebral localization. He continued to think in vague terms of the "nervous energy" of his youth, as if a certain quantity of this commodity were released and had to flow somewhere—if it were not allowed to take one channel it would take another. In a paper addressed to the Academy of Medicine the year before his death he argued that return of sensitivity and movement after suture of nerves is merely a matter of replacement of "inhibition" by "dynamogenesis," "a simple dynamic change, a transformation of force, which has taken place."[10] One must admit that although we consider ourselves more fortunate in our more modern explanation, when instead of "nervous force" we prefer to think in terms of concentration of excitatory and inhibitory substances released at nerve endings, the problem of facilitation and inhibition is still far from a complete solution.

Brown-Séquard's own feelings regarding his fight for these theories of nervous action, in defence of which he stood virtually alone, defying all other reputable neurologists, are shown in a letter of 1879

to his English friend, Dr John W Ogle (1824-1905) He wrote

My lecturing and some patients take all my time I have a very much harder fight for the doctrines relating to the brain than I had at the time I first became acquainted with you for doctrines relating to the spinal cord If I did not love truth much more than comfort, ease and quietness, I should give up the painful heavy task I have given myself So long, however, as I have a breath of power of mind or body, I shall continue the efforts begun in London in 1861 in my Gulstonian lectures

No one can accuse Brown-Séquard of lack of purpose, and particularly of lack of tenacity

Honors and prizes came to him in the course of his work at the *Collège de France*, the Legion of Honor in 1880, an honorary LL D from Cambridge University in 1881, the Baly medal from the Royal College of Physicians in London in 1881 Also in 1881 he secured the Montyon Prize for d'Arsonval (a peace offering after the quarrel?), and he himself was given the Lacaze Prize, the most distinguished award in the gift of the Academy of Sciences

When Vulpian presented his report on the Lacaze Prize, he enumerated what the committee had considered Brown-Séquard's most notable contributions

to science these were (1) demonstration of the crossing of sensory impulses in the cord so that sound diagnosis of certain pathologic states in man was possible, (2) his experiments on irrigation of dying tissues by blood, suggesting that severed limbs might be reanimated, (3) his demonstration that vasomotor nerves respond to electrical stimuli, (4) production of epilepsy in animals ("an entirely new fact," said Vulpian) and its transmission by heredity, and (5) demonstration of inhibition by which lesions of the central nervous system affect nervous centers at a distance

This estimate by his contemporaries is surprising in two respects, the work on the suprarenal bodies was not considered worth mentioning, while that on artificial epilepsy and its transmission by heredity was regarded as the field in which he displayed his greatest originality Since this verdict places the work on epilepsy and heredity on a level with contributions of which the value cannot be challenged, it will be permissible at this point, although reference has already been made to the more clinical aspects of the subject, to go back to trace the development of his ideas and give our own estimate of their significance

2

His first paper on epilepsy appeared in 1850[11] The results which he reported at this time under the title, "On the convulsive disorder displayed in animals having the lateral half of the spinal cord cut," were a sequel to his very earliest experimental work He had noticed that some eight to ten days after the operation of hemisecting the cord in guinea pigs between the 8th dorsal and the 4th lumbar vertebrae, the animals would go periodically into convulsions The muscles of the face, of both front legs, and of the hind leg on the side opposite to the lesion would jerk violently The seizures became most violent four to five weeks after the operation, the crises lasting some fifteen minutes, the animal becoming unconscious, and exhaustion being so great that a second convulsion would not occur before several hours rest The peculiar feature of the whole procedure was that some change seemed to have taken place in the skin in the region about the face and neck on the side of the lesion, so that pinching in this area would bring on a convulsion Because of its special sensitivity he designated the

area the epileptogenic zone." These findings are most puzzling for, with the spinal cord hemisected so far caudad, it is impossible to see how cutting off sensory impulses from one hind leg, or motor impulses to the other could possibly affect the skin on one side of the face and neck that a mere pinch there would set off a violent epileptic fit. This aspect of the phenomenon seems certainly to imply "nervous action at a distance."

The next paper was a short one appearing in the same year[11] in which he stated that he had found that he could produce convulsions by pinching the skin on either side of the face when the cord was completely transected instead of being hemisected. This time, of course, there were during convulsions no movements of either hind foot, but the muscles about the neck and face were violently contracted.

In his American lectures of 1856 he reported[12] that the epileptogenic zone was confined to the skin, since he was unable to cause convulsions by direct stimulation of the branches of the 5th cranial nerve going to this region of the cheek. Furthermore, the convulsions did not result from pain aroused by a pinch on the skin of the zone, because the zone was, he insisted, actually less sensitive than other parts of

the skin The loss of consciousness he laid to contraction of the blood vessels of the brain through action of the great sympathetic nerve These results were obtained at the time when he was completing Bernard's story of vasomotor fibers in this nerve One point which he brought out in these American lectures is most suggestive He had found that cauterization by hot iron of the epileptogenic zone would cure the animal of its seizures, and he added, "There is something of the same kind in the condition of the skin of the neck and face in these animals, and in parts of the skin which are a seat of a true *aura epileptica* in man" The success of the drastic measure of cauterization in animals led him to advocate its use in man, and he later lamented that this treatment was not more often used on human patients He said in his lecture before the Royal College of Surgeons in London, May, 1858

As regards this treatment of epilepsy, we will only say that the principal rule is to find out if the disease has an external cause—i e, if from any part of the centripetal nerve there is an irritation acting upon the nervous centers To prevent this irritation reaching these centers, or to destroy the cause of irritation, if it is known to exist, are the two things to be done I must repeat that this will be

found much more often than is generally supposed Against the increased excitability of some part of the nervous centers, the best means, assuredly, are the powerful modificators of nutrition, which, I am sorry to say, are so little employed by regular practitioners—the cauterization of the back of the neck by moxas [14] or by the red hot iron

In 1856 Brown Séquard summed up the results of all the experiments on epilepsy which he had been making over the last six years in the intervals between his ocean journeys, and incorporated them in a formal report before the Academy of Sciences [15] One statement in this report should have given him pause He said that if the operated guinea pigs were confined in a narrow space and were well-fed, they had more frequent and violent convulsions, even fifty spontaneous seizures in a day If, however, they were kept in an open space, and their diet was adequate but restricted, there were not only no spontaneous convulsions, but convulsions were hard to induce artificially by irritation of the epileptogenic zone Disregarding this and all other disturbing aspects of his data, he held firmly to the theory that all could be explained as an excitation passing from the site of the lesion in the cord to the pons in the brain, parts anterior to the pons, he thought, did not

enter into the picture, since he could remove all the forward parts of the brain down to the pons and still induce convulsions, in the pons the roots of the 5th nerve were so affected that their excitation was enhanced and their reflex properties so exaggerated that blood-vessels of the head were contracted, the face became pale, the pupils dilated, and asphyxia resulted because return of the blood was prevented by the strong contraction of neck and chest muscles, it was, in his opinion, the increase in carbon dioxide of the blood which furnished the final stimulus to set off the motor elements of the cord and brain and also produce unconsciousness He had worked out a complete theory on the basis of his data, and, like many another scientist, was seduced by the very completeness with which his theory seemed to cover the facts into regarding it as no longer needing to be tested, to be verified It was against this very attitude that Bernard was shortly to sound a warning in his *Introduction to Experimental Medicine*

While these operated guinea pigs were being kept under observation, because, as in Ellis Parker Butler's famous story, " pigs is pigs," they multiplied in their customary manner Brown-Séquard began to note signs of epilepsy in their offspring This observation

was first announced to the *Société de Biologie* in 1859.[16] He was cautious enough to say that not all parents suffering from artificially induced epilepsy had epileptic young, nor were the manifestations always exactly the same in the offspring as in the parents, but he did state that he never saw, in all the immense number of guinea pigs he had handled, a single case of spontaneous epilepsy unless one of the animal's parents had been rendered epileptic through an operation on the spinal cord. He admitted that the actual lesion could not be transmitted by heredity, but he reasoned that the offspring must have inherited "an alteration in the general organic disposition of the nervous system." In order that the English, who were not overinclined to read articles in a language other than their own, might know of his observation, he at once sent to the Royal Society of London a brief note in which he announced without qualification that epilepsy, or an affliction closely resembling it, could be transmitted to their offspring by parents in which this state had been artificially produced. This statement, which appeared in the *Transactions of the Royal Society* in 1860,[17] so impressed Charles Darwin (1809-1882)

that in the first edition of *The Variation of Plants and Animals under Domestication* (1868) he wrote

> But perhaps the most remarkable and trustworthy fact is that given by Dr Brown-Séquard that many young guinea pigs inherited an epileptic tendency from parents which had been subject to a particular operation, including in the course of a few weeks a convulsive disease like epilepsy, and it should be especially noted that this eminent physiologist bred a large number of guinea pigs from animals which had not been operated on, and not one of these manifested the epileptic tendency On the whole we can hardly avoid admitting that injuries and mutilation, especially when followed by disease, or perhaps exclusively when thus followed, are occasionally inherited

Brown-Séquard resumed his experiments on epilepsy in 1869 in Paris, while he was occupying the chair of Comparative Pathology, and the striking point which he added in this year was that merely cutting the sciatic nerve in one hind leg would create an epileptogenic zone about the face and neck on the side opposite the cut nerve Out of a clear sky and with no further comment he added this observation " Lice will accumulate on the skin in this zone, even though the animal can scratch at this point, only it must be stated that lice do not exist on white parts

of the skin, so that if the epileptogenic zone were formed only of skin with white hair, it would be useless to wait to find lice there" [18] What significance he thought this statement had is not indicated in any way in this paper It appears to record a chance observation for its own sake

Again in this year he emphasized the parallel between the epilepsy of his guinea pigs and that in human cases, since in man he had observed that it was often necessary that a single spot be irritated in order to set off epileptic seizure

In 1870 he went over all his results again and added to the list of mutilations that would lead to epilepsy lesions in the brain even anterior to the pons He also claimed that he had demonstrated that a physical character can be transmitted from the father to the mother *via* the offspring This is indicated in a tantalizing report by the secretary of the *Société de Biologie* for its first meeting after the New Year's holiday of 1870 that Brown-Séquard displayed two guinea pigs "in which, according to all appearances" (these are the words of the cautious secretary) "there has been transmission by heredity of an alteration artificially acquired by their sire" What this alteration was is not stated, but in

a subsequent report some months later we find that it must have been alteration in the shape of the ear of a guinea pig whose father had a similar modification as a result of gangrene following section of the sympathetic nerve in the neck Strangely enough, the mother, although unoperated, had a similar deformity of the ear, although to a lesser degree Brown-Séquard presented this case as an example of what he said " an Englishman of our own time, a Mr Harvey " had already demonstrated, *viz* , that a physical character can be transmitted from the father to the mother *via* the offspring This announcement brought a storm of protest [10]

In the course of the discussion which was carried on for several meetings Paul Bert said he had removed the eyes from four generations of rats and the young still had eyes, and he called to mind certain age-old customs, such as circumcision, where surgical procedures certainly had had no hereditary effects Vulpian and Phillipeaux reported that they had removed a single testis, the spleen, and other organs in animals with no transmission of the effects to succeeding generations All were inclined to think the cases cited by Brown-Séquard were coincidences from accidental causes That investigator's own

views were reinforced rather than weakened by this opposition, and before June he had made seven communications on cases of transmission of mutilations, such as alterations in the ear and in the feet (including loss of toes)

Since Brown-Séquard crossed to the United States in 1870, one wonders what became of his colony of guinea pigs during the Franco-Prussian war, for we know what happened to some Parisian dogs and rats at this time It may be that one can detect a sorrowful note in his remark of a few years later when he said that just before the siege of Paris he had in his laboratory 584 guinea pigs At any rate, on his way overseas he took occasion to look in upon the Liverpool meeting of the British Association for the Advancement of Science in September, and to present a paper, which is reported by title only, on inheritance of acquired characters The impression on English scientists was profound Darwin in his next book, *The Descent of Man* (1873), said, "We now know from Dr Brown-Séquard's remarkable observations, especially those communicated (1870) to the British Association, that with guinea pigs the effects of operations are inherited," and in the next edition (1875) of his more famous *Origin of Species by*

Natural Selection Darwin now included a reference to the "remarkable cases, observed by Brown-Séquard, of the inherited effects of operations" It is no small distinction to have one's work cited in three of the most famous books in the whole literature of biology, although the honor is somewhat diminished by the scepticism of later generations of scientists regarding the validity not only of the conclusions but of the observations on which these were based It may be observed in passing that Brown-Séquard's name also appeared in the current editions of a famous philosophical work of this period, John Stuart Mill's *System of Logic* In book III, on induction, Mill used as one of his examples to illustrate the Method of Difference Brown-Séquard's experiments on *rigor mortis*, and as an example of the exploration of natural law his work on reflexes

Back in Paris again in 1872, Brown-Séquard announced before the *Société de Biologie* that when he cut the sciatic nerve in guinea pigs in the United States there were no signs of epilepsy such as he had found when he cut this nerve shortly before leaving for America Could it be an effect of the climate, he asked After making this astounding report he proceeded to section the sciatic nerve in each of two

French guinea pigs, and only one guinea pig developed epilepsy, and at that, later than usual, after three months interval, and the epileptogenic zone was not exactly in the customary position. His explanation for the complete failure in the one case was that the sectioned sciatic nerve had united more rapidly than usual and he was inclined to think that a more rapid rate of regeneration would account for his failure to produce epilepsy by sectioning the sciatic nerve in American guinea pigs. For some reason nerves must unite faster in union there than in France. This, it must be remembered, was after the siege of Paris, and I am inclined to think that he had had to start a new colony, so that the inbreeding (and perhaps other characteristics) were different from what had prevailed in his former colony.

The blame which he had originally placed upon the climate of the United States for his discordant experimental results had been displeasing to Claude Bernard, who, as president of the *Société de Biologie*, was presiding at the meeting where Brown Séquard made his report. Bernard commented, after hearing this new explanation of Brown Séquard's failure to produce epilepsy in American guinea pigs, that he "approved of the tendency in science not to be

content with vague expressions of the influence of climate, but to try to explain this difference" This led to a question by M Bergeron whether there were fewer epileptics in America than in France To this Brown-Séquard replied, "If one may judge by the number of patients who consulted me in America, I am led to believe that there are incomparably more epileptics in America One of the causes which would explain this fact is the abuse of tobacco, perhaps also the use of stomach excitants, such as cayenne pepper As to absinthe, it cannot be blamed, since this liquor is unknown, save perhaps in New York The extreme dryness of the climate renders the excitability of the nervous system very great" It will be seen that Brown-Séquard had in reality not abandoned his idea that difference in climate was at bottom responsible for vagaries in the nervous systems of men and beasts resident in these United States of America

The problem of nervous pathways involved in his experimental epilepsy remained baffling Because he found that cutting the cord immediately above the origins of the sciatic nerve did not produce epilepsy, whereas pulling the nerve out by the roots did, he was inclined to think that it was not the

damage to the sciatic *per se* which let loose this mysterious effect, but it must be the severing of sympathetic fibers which run along with the sciatic. At the time he made this report he was afraid that the difficulty in separating the sympathetic from the somatic fibers would prevent him from making a clean-cut experiment on this point. Bernard, who was all enthusiasm over this idea, because anything concerning the great sympathetic nerve was of especial interest to him, suggested using a dog for the experiment, but Brown-Séquard replied that neither the dog nor the cat are good subjects to try to render epileptic. He persevered with his guinea pigs and was able to demonstrate before the *Société de Biologie* in 1872 that after cutting the abdominal sympathetic, irritation of the epileptogenic zone would cause convulsions, but the experiment was tricky, since excitable spots were hard to find and they varied not only in individual animals, but in the same animal at different times.

Paul Bert interjected a very pertinent question after Brown-Séquard made this report. He asked whether a simple skin or muscle injury was not sufficient to make guinea pigs have convulsions, for it was said that merely placing a bit of wood or

elder pith beneath their skin would render them epileptic This tendency of French guinea pigs to have convulsions so readily under so many different conditions had evidently aroused Paul Bert's suspicions as to the specificity of the means which Brown-Séquard employed to produce the state of epilepsy But Brown-Séquard replied that although he had not put pieces of wood under the skin of his guinea pigs, he had put pieces of bone, and there were no convulsions He was now definitely committed to the idea that the sympathetic nerve was responsible for epilepsy, and as proof that the sympathetic could be affected by so remote an influence as cutting the sciatic, he presented before the *Société de Biologie* two guinea pigs which showed pronounced exophthalmos on the side on which the sciatic had been cut

Although, on the face of it, the production of permanent unilateral exophthalmos by cutting the sciatic nerve in the thigh of the guinea pig seems rather a far-fetched idea, Claude Bernard was very pleased with it, and he clarified the situation with one of his beautifully succinct statements which appeared to tie the whole thing neatly together "In order to explain exophthalmos in these guinea pigs," he said, "one must assume that there is,

following the section of the sciatic nerve, a permanent excitation of the central end, leading as a consequence to a permanent excitation of the great sympathetic nerve." Such permanent excitation we know may occur when the central end of the nerve, instead of making union with the peripheral stump, becomes lost in scar tissue. It seems, however, more probable that if this were the case in Brown Séquard's experiment, this excitation would lead to a reflex involving both eyes rather than one. Ingenious is Bernard was in trying to help out his rival in his explanation of his data, we still remain incredulous.

One remarkable feature about the effects of cutting the sciatic nerve is reported by Brown Séquard must be mentioned. It will be remembered that he claimed that immediately after the operation the epileptogenic zone in the face and neck became less sensitive than other parts of the skin to mechanical or electrical stimulation, but a pinch here would set off an epileptic convulsion. Now he claimed that while the cut ends of the sciatic nerve were uniting three very peculiar things happened. (1) the skin in the epileptogenic zone recovered its sensitivity, (2) the epileptic fits diminished in intensity, and (3), most remarkable of all, the hair began to fall out in the

epileptogenic zone The beginning of the fall of hair about the face and neck signalized, he said, the beginning of the union of the sciatic nerve in the leg[1]

In 1875, at the period of his greatest personal distress and indecision, he published in the *Lancet* a summary in English of all his work to date on the inheritance of acquired characters This summary was quoted in detail by English writers on heredity for the next fifty years Some accepted the evidence, for example, George John Romanes (1848-1894), in his *Darwin and After Darwin*, a work in which he fearlessly carried on the torch of evolution lit by Darwin, considered Brown-Séquard's the "best-known" researches yielding evidence for the transmission of acquired characters, and because Brown-Séquard said that he never observed these characters in any of the thousands of animals which had passed through his hands, whose parents had not been operated upon, Romanes was willing to state that in Brown-Séquard's work "the hypothesis of coincidence, at all events, must be excluded" When, however, he tried himself to repeat Brown-Séquard's observations, he did not meet with full success This was some fifteen years later and the story, which

is preserved in d'Arsonval's published correspondence, is as follows [20]

After he came to the *Collège de France* Brown-Séquard made it a rule that no one except his official assistants should be allowed to work in the laboratory furnished by the *Collège* while he was away spending his winters in Nice, but he was willing to make an exception in the case of his old pupil, Dupuy, in order that he might demonstrate to Romanes certain operational procedures In the winter of 1890, the distinguished visitor had come to Paris from Edinburgh, where he was just finishing a special four-year lectureship before taking up his final residence in Oxford Unfortunately Brown-Séquard had forgotten to inform d'Arsonval, who was always in charge in his absence, of the arrangement he had made before leaving Paris, and Dupuy was refused permission to prepare the animals for the demonstration In a letter to d'Arsonval, dated December 29, Brown-Séquard wrote the following authorization

> You are to give him (Dupuy) permission to go into the part of the laboratory which used to be an outhouse, and you will receive with your customary courtesy the learned biologist who will come soon to see Dupuy's work I enjoin you to let Mr Romanes see everything, and you will find

him at the same time well-informed and very intelligent, and you will express to him my lively regret not to be there to do him the honors of the laboratory Most affectionately yours

Romanes reported later that the assistant whom he saw perform the operation of wounding the restiform body had so careless a method of doing it that when he came to repeat it for himself he got uniformly negative results Altogether, he said, he lost two years of work, and was finally forced to go to Paris again, this time for the express purpose of seeing the master himself perform the operation, although Brown-Séquard was seventy-five years old at this time Romanes' repetition of the experiments gave so many negative results that he had to admit,

On the whole, then, as regards Brown-Sequard's experiments, it will be seen that I have not been able to furnish any approach to a full corroboration But I must repeat that my own experiments have not as yet been sufficiently numerous to justify me in repudiating those of his statements which I have not been able to verify

Other writers, for instance, J Arth[illegible] Thomson (1861-1933) in his *Heredity* (1908), quoted Brown-Séquard's summary in the *Lancet* of 1875 only to criticize each point adversely Thomson's final com-

ment was that although Dr Brown-Séquard was "a skilful and ingenious, if somewhat impetuous physiologist our general conclusion is that the results of his experiments do not strengthen the affirmative position" The weight of Brown-Séquard's name was still sufficient to cause some hesitancy in pronouncing flatly against him The verdict was reminiscent of the Scottish "Not guilty because not proven, but don't do it again" By 1930, however, there was no one who would not admit with Professor E Guyénot in his *La Variation et l'Évolution* that "as to the so called transmission of anomalies in feet, eyes, ears, etc, it rests simply on the fact, well-known to all those who have raised guinea pigs, that these animals present spontaneously, and precisely in the proportions stated by Brown-Séquard, diverse anomalies or congenital malformations" At the present time authors have ceased to quote Brown-Séquard on the now defunct subject of inheritance of acquired characters, or if they do mention him, they do so as a matter of historical interest in a mistaken and disproved theory

The article in the *Lancet* in 1875 is particularly noteworthy to me for the claim made there that in two guinea pigs, both of them epileptic and both

lacking toes because their parents had had a sciatic nerve cut, there was observed the same sequence of morbid states as in the parents from the time of cutting their sciatic nerves until the reunion of the cut ends, *viz*, recovery of sensitivity in the epileptogenic zone, diminishing intensity of convulsions and falling of hair from the face and neck This extraordinary "inheritance" by two animals with intact sciatic nerves not only of the same series of morbid symptoms as their parents, but even of the order in which they had originally occurred in the operated animals, should surely have made an unprejudiced observer somewhat doubtful of his ground But Brown-Séquard had made up his mind in 1859, he did not thereafter change it His first observations had been made in the era when anecdotes and hearsay were used as evidence in questions of heredity, and carefully controlled experimentation and application of rigid statistical methods had not come into use His attitude was, therefore, that every piece of evidence which he could muster should be made to tell for his side of the argument Like Darwin, he cited cases of what to us now seems to be pure coincidence He told of a man with an accidental scar like a circumflex accent on his jaw,

each of whose three daughters had a similar disfiguration, of a man with his middle finger missing, two of whose grandchildren were born lacking a middle finger, of a shipboard acquaintance on a return voyage from America who had had a finger amputated and whose son, born four years later, had two fingers missing. He even showed the *Société de Biologie* a case of compensatory heredity, a guinea pig with supernumerary toes, born of parents lacking the ordinary number of toes. In reporting this last case of so called "heredity" he did save his reputation for sanity by stating again the principle that "an animal did not inherit an external lesion, but only the particular state of the nervous system which determines these effects."[21]

The most complete list of the inherited characters which Brown Sequard claimed to have demonstrated by his experiments is to be found in his last formal paper on the subject, a communication made in 1882 to the Paris Academy of Sciences.[22] I shall quote this list in preference to the better known one, taken from the *Lancet* of 1875. According to the later enumeration, the list of inherited characters which he had observed is as follows: (1) Epilepsy in animals born of parents which had been rendered epileptic by

section of the cord or of the sciatic nerve, (2) Change in the shape of the ear, or partial closure of the lids when the parents had had the cervical sympathetic cut, (3) Exophthalmos when the parents had had lesions in the medulla, (4) Ecchymosis and gangrenous ears when the parents had had lesions in the restiform body, (5) Absence of phalanges or nails when the parents had lost these organs as a consequence of section of the sciatic nerves, (6) Appearance of the epileptogenic zone in animals whose parents had been rendered epileptic through having the sciatic cut, and the falling of hair as the epileptic symptoms abated, (7) Opacity of the cornea, lens and vitreous humor in offspring of parents with injury to the restiform body, (8) Muscular atrophy in offspring of parents with the sciatic cut

It is to be noted that Brown-Séquard clearly stated that operated parents do not *of necessity* transmit such defects, they appear in about two-thirds of the offspring of parents with accidental lesions, but once appearing, he said, the defect could reappear for five to six generations This seems to be his final word on the subject of inheritance of acquired characters, and unless the future brings forward some cataclysmic evidence in favor of this theory, I am

afraid that we shall continue to consider his whole list as accidental coincidences in a type of animal prone under laboratory conditions to show such deficiencies spontaneously

In his old age Brown Séquard continued his investigation of guinea pig epilepsy in its own right, as distinguished from the studies in heredity, originally a branch of the earlier studies in epilepsy, but in the end almost dwarfing the tree His last experiments were done when he was about seventy five years old The report of them was given at the Academy of Sciences in 1892 and was entitled "Notes on some new facts relative to the physiology of epilepsy" [23] The new facts were that amputation of the entire hind leg of the guinea pig at the hip led to much more complete and lasting epilepsy than merely cutting the sciatic nerve, since with complete amputation there was no possibility of regeneration of the nerve taking place to prevent the appearance of epilepsy He found that amputation below the knee was not so effective and the results were transient The particular point which he wished to emphasize in this paper was that before an animal could be considered epileptic there must be produced a morbid state which predisposed to the appearance of con-

vulsions and loss of consciousness, and that this process was distinct and separate from the immediate cause of a single epileptic attack Again in this paper he drew a close parallel with human epilepsy, and his final word was, " I have shown by clinical facts as well as by experimental facts that epilepsy has no special seat in the brain, that all parts of the nervous system, central and peripheral, can produce this condition " The statement that epilepsy has no special seat in the nervous system would still stand today in the case of the so-called " ideopathic epilepsies," but not, of course, for " Jacksonian epilepsy," which, implying as it does the validity of the theory of cerebral localization, was never acknowledged by Brown-Séquard

When we survey critically the whole series of Brown-Séquard's experiments from 1850 to 1892 in an attempt to arrive at what we may call the physiology of his " artificial epilepsy," we not only feel that he did not succeed in saying the last word on the subject, but that there are too many inconsistencies in the picture for us to be satified with it at all as he conceived it It does not seem reasonable from what we know of the physiology of the nervous system that any one of the following procedures, cutting

the sciatic nerve, amputating the leg, hemisecting or completely transecting the lower spinal cord, pricking the cord at the base of the brain, destroying various parts of the brain anterior to the pons, and cutting the abdominal sympathetic, would in every case render the region around the exit of the 5th cranial and the first two cervical nerves so sensitive that a gentle pinch on the skin of the neck and face of the guinea pig would set off a convulsion of a particular type and result in unconsciousness, that this would not occur in American guinea pigs, but only in French ones, and then only if they were crowded together and well fed, and finally, that cauterization of this area, or merely cutting away the skin, would abolish the tendency to convulsions. These results do not appear to fit together at all, but they seem to have been accepted for the next fifty years, since "experimental epilepsy" is still cited as one of Brown-Séquard's crowning achievements.

Today, however, to add further to the perplexity of this confusing century-long story, we have the recent experiments of Pagniez and Pichet, begun in Poland and continued in Paris.[24] They, too, find that cutting the sciatic nerve in their guinea pigs produces an epileptogenic zone and Brown-Séquardian epi-

lepsy, but—and here is the revelation—on these guinea pigs there must be a plentiful supply of lice of a particular species, *Gyropus ovalis* Other more common species of lice, such as *Menopon extraneum*, will not produce disposition to the epileptic state or furnish an epileptogenic zone Delousing the guinea pig abolishes the epileptogenic zone and puts an end to the fits Even allowing *Menopon* to overpower *Gyropus* in numbers will abolish the previously established epilepsy The point about the mutilation is that the guinea pig with a paralysed hind leg or no hind leg at all simply cannot scratch its face and neck Hence the lice accumulate in this area in great numbers as Brown-Séquard observed, he, however, thought the lice accumulated there whether the guinea pig could scratch or not Why should this particular louse produce so weird an effect on the nervous system, and why should pinching the skin in an area specially loaded with lice set off an epileptic fit?

It has been suggested to me by Dr Morris A Stewart, parasitologist at the University of California, that this louse, like certain ticks, may produce a neurotoxin and that this may be the source of all the neurological manifestations It is a disconcerting

reflection that one whole aspect of Brown-Séquard's career was virtually determined by a louse, of the existence of which he was certainly aware, although not of its potentialities If his guinea pigs had not been infested with this particular type of louse, he might never have embarked upon his life-long studies in epilepsy, he certainly would not have been led into his unprofitable investigation of the inheritance of acquired characters, and, in all probability, he would not have formed his erroneous views on action at a distance as an explanation of the effects of lesions to the nervous system The modern experiments, it is true, confirm his observations, and we are left with the problem of pronouncing judgment upon his interpretation of his data The root of the difficulty, here as elsewhere, was his attachment to his theory of action at a distance He might have fared better if he had followed the advice of Claude Bernard, who said that a scientist should leave his theories outside the laboratory, as he would his overcoat Brown-Séquard's habit of mind was really closer to that of Darwin, who said, "To observe profitably one must first have a theory" One might go further and say that this dictum had done equally bad service to both scientists who followed it

3

To return, after this long digression, to the work going on in the laboratory at the *Collège de France*, we find that in 1882, as in 1881, papers on inhibition continued to appear One of the most interesting reports of this year was on the special influence of the nervous system in modifying exchanges between blood and tissues in traumatic shock and similar conditions This was prophetic of the intensive work on this subject during the two world wars Brown-Séquard was evidently dealing with "primary" rather than true "traumatic" shock, since he thought that he had established that the nervous system under these conditions prevented exchange between blood and tissues, his evidence being presence of oxygenated blood in veins, and lowering of body temperature [25] More work on stimulation of different parts of the brain strengthened his conviction that "all value was lost" for the theory that one side of the cerebral cortex controlled the opposite side of the body, "it must be admitted that one motor zone and any excitable part affect both sides of the body" [26] For a time, use of carbon dioxide as an

anesthetic particularly of the larynx, engaged his attention.

In 1882 Paul Bert, as Minister of Instruction, created for d'Arsonval a new laboratory at 12 rue Claude Bernard, but still under the auspices of the *Collège de France*, the director himself sharing it with Brown-Séquard and d'Arsonval. This laboratory was expressly for d'Arsonval's specialty, biophysics, but he carried on there also investigations initiated by Brown-Séquard. Claude Bernard's old laboratory, the Laboratory of Medicine on the rue des Écoles, became more or less the adjunct of the lectures given in the *Collège de France*. In 1883 Brown-Séquard, who was now sixty-six, inaugurated his custom of taking refuge for the winter in Nice from the inclement Paris weather. The winter course of lectures was entrusted to d'Arsonval, who dealt with his own subject, electrophysiology. A seasonal rhythm was established, whereby Brown-Séquard returned to Paris every spring in March or April, took a mid-summer holiday on the Channel coast, spent some of the autumn months in Paris and was back in Nice by December. D'Arsonval took midsummer vacations on the country property which he had inherited, Laborie, near Limousin, sometimes extending his

stay late into the autumn A number of invitations were proffered on both sides to visit the vacation homes, but apparently no such visits ever actually took place

In the summer of 1884, while Brown-Séquard was in Dieppe, d'Arsonval, who was inclined to concern over his own health, became worried about the cholera and received excellent advice from his chief to live hygienically, to use only freshly boiled water, if symptoms did appear, " there is no shadow of a doubt that opium is a true antidote of cholera " At this time Brown-Séquard seems to have been toying with the idea of giving the winter lectures himself that year, but by October it was decided that d'Arsonval should continue He wrote to announce his subject for 1884-1885 and added that electrophysiology " needed to be freed from German nebulosities and the fanciful theories of M Dubois-Reymond " [28] The same letter shows the interest with which Parisian scientists followed the activities at the laboratory D'Arsonval wrote

I spent the morning with Pasteur who had much to say about you Your experiments on carbonic acid and stoppage of exchanges interested him greatly The action of the nervous system on the phenomena of putrefaction

have (*sic*) completely fascinated him He believes like you in the secretion of a disinfectant liquid and showed me analagous effects on animals which he had inoculated with the virus of rabies He claimed that he had failed greatly and that he was aware of this by the infallible sign that he was becoming dogmatic and was inclined to be pontifical

Pasteur (1822-1895) was at this time sixty-two years old and had just begun his experiments on hydrophobia

In 1885 Brown-Séquard was given the Lallemand Prize of the Academy of Sciences for his work on "Inhibition and Dynamogenesis" This was the Grand Prix of 20,000 francs given biennially Paul Bert made the report The examples which he took from Brown-Séquard's work on inhibition included the following when a strong current of carbon dioxide is directed on the larynx its stops respiration and suspends general sensitivity and this action is inhibited by excitation of the superior laryngeal nerves, convulsions of an attack of spinal epilepsy may be inhibited by pulling on the nail of the big toe As an example of dynamogenesis he cited the finding that section of one-half of the spinal cord exaggerated the excitability of the same side of the cord above the cut

The next year, 1886, Brown-Séquard finally obtained a chair at the Academy of Sciences when that of Vulpian became vacant upon the latter's appointment as Permanent Secretary When it was made known that Brown-Séquard had finally been awarded a place in this Academy, a deputation of Mauritians living in Paris came to congratulate him To show that he was not forgotten in the island itself, he was made on August 6 honorary president of the *Société Médicale de l'Isle Maurice*, and the governor of the island recommended to the British Government that he be given the Cross of St Michael and St George, although nothing ever came of this

Then Paul Bert, who had succeeded Bernard as President of the *Société de Biologie*, died The letter which Brown-Séquard wrote to d'Arsonval shortly afterwards intimates that Brown-Séquard had been offered the presidency of the *Société*, then the offer was withdrawn and Chauveau asked to serve The reason for this seeming affront was the finding of a letter which Brown-Séquard had written to Paul Bert a few months before saying that he desired only to be vice-president along with Chauveau The letter had been written merely to facilitate the business of

the society on the assumption that Paul Bert was to remain president Brown-Séquard wrote

To use me so, now that Bert is dead, and have me nominated vice president without Chauveau is an act of unqualifiable jesuitical fraud P S— *If the Société de Biologie elects me president, even by a majority of one vote, I shall accept*

The postscript was underscored The voting took place March 26, 1887, and Brown-Séquard won over Chauveau 42 to 15 He said that he cherished the honor above all others which had come to him in his lifetime, but, although he was now seventy, he was not permitted, like his predecessors to end his term of office only with his death Evidently by this time it was felt that to elect a president for life was not giving others a fair chance, for beginning with Brown-Séquard the term of the presidency of the *Société de Biologie* was limited to five years An anonymous contemporary later described his assiduous attendance at the society's meetings during the season of his residence in Paris, and his tendency to remark when a communication was made, " In 1842 (or in 1845) I observed the phenomenon which has just been described," and this not in any spirit of

claiming priority, but merely to confirm the precision of the observation The same writer says that his eyes, always bright, sparkled still more when the conversation turned to a scientific point, that his manner to younger scientists was kindly and without condescension [29] An agreeable duty, before he had held his presidential office many months, was the introduction to the *Société* of His Majesty, the Emperor of Brazil, with the characterization, "a sovereign eminent for the finest qualities that man can possess, and above all for his profound love of the sciences" Some years before the Emperor had been conspicuous in the audience for Claude Bernard's lectures at the *Collège de France* So much did Brown-Séquard in his turn appreciate the royal friendship that he even consented to have his photograph taken in order to present Dom Pedro with a copy Ordinarily he detested having his portrait taken, apparently because he disliked the idea of having copies of it sold or distributed He permitted it to be done only once or twice [30]

Their work on carbon dioxide led Brown-Séquard and d'Arsonval to further investigation of gases D'Arsonval planned a special chamber, following the design of the famous one used by Pettenkofer

(1818-1901) and Voit (1831-1908) for their studies in metabolism, and providing it with a special ventilating system The result of work on this subject was a series of papers in which the collaborators thought that they had shown that toxic materials are given off in the breath, and it was this toxic material which rendered air breathed in a confined space so harmful When this poisonous substance in the expired air even of healthy persons or healthy animals was injected under the skin or into the blood of another animal it produced toxic effects of such a nature that the investigators were sure that it was "not a microbe but an organic alkaloid analogous to the ptomaines" They therefore recommended constant breathing of pure air for phthisis patients, and were gratified to receive from physicians as far away as James Blake (1815-1893) in California reports of success with the open air treatment of the tubercular [81] D'Arsonval had plans for some apparatus which the physician could take to the home of the city-dwelling patient, so that even he could breathe uncontaminated air This led to a study of the ventilation of hospitals, and Brown-Séquard so interested the authorities of the hospital in Nice that they asked d'Arsonval to make a plan

for the better ventilation of their wards [32] The subject was very much in the limelight at this time because of the first International Congress for Tuberculosis held in Paris, July 25-31, 1888 Brown-Séquard's colleagues in Paris, however, were quite sceptical regarding the toxic materials in expired air Dastre (1844-1917) and others failed to find any such toxic product The minutes of the *Société de Biologie* for 1888 are filled with objections to the idea and with replies to the objections Even before Brown-Séquard -and d'Arsonval had begun their experimental work, one of the pioneers in research on tuberculosis in America, Edward Livingstone Trudeau (1848-1915), had shown in his small laboratory at Lake Saranac that with experimental animals mere confinement, bad air and restricted diet could not produce tuberculosis unless the bacillus itself were present It is true that the fresh air treatment proved to be greatly beneficial for the tubercular, but it is extremely doubtful that the beneficent effect was the result of avoidance of toxic exhalations

Although the laboratory at the *Collège de France* fairly buzzed with activity (Dupuy as well as d'Arsonval participated, and, to quote d'Arsonval

writing in 1883, slew his "hecatombs of dogs"[33]) no project was thought through with the calm critical logic of the time of Claude Bernard, and the lasting contributions made in the 80's and the 90's were relatively few

4

No more spectacular finish to a spectacular life could be imagined than the last phase of the activities of Brown Séquard One would expect that at the age of seventy-two he would have been content with the achievements of fifty years' incessant investigation, and would have been willing to leave to his competent assistant, who since 1887 had had the title of *professeur suppléant*, not only his lectures at the *Collège de France*, but the laboratory work as well But that was not Brown Séquard's temperament Lectures, except as the exposition of his own discoveries, did not interest him, but experimental projects were another matter If he had arrived at the age when man's powers begin to wane and indications of senility to show, on what better subject than himself could he try out his ideas of 1869 regarding the possibilities of rejuvenation? D'Arson-

val should apply his inventive genius to devising special methods of preparing the rejuvenating extracts, and the aging professor would this time himself serve as the guinea pig for testing their potency

The first announcement of the daring experiment was made before the *Société de Biologie*, June 1, 1889 What Brown-Séquard had done was to give himself during the previous fortnight six subcutaneous injections of small quantities of a water extract of ground-up testicles of dogs or guinea pigs D'Arsonval had made sure that the extract contained no bacteria, and although the site of injection remained sore for a week, there were, according to the subject's own statement, astonishingly beneficial effects He reported

I was 72 years old the 8th of last April My general vigor, which had been considerable, has diminished notably and gradually during the last ten or twelve years Before the experiments, which now occupy me, I had to sit down after standing for an hour working in the laboratory After three or four hours, and sometimes after only two hours of experimental work at the laboratory, although I sat down, I was left exhausted On returning home by carriage about six o'clock in the evening, after some hours passed thus in the laboratory, I was for many years so tired that I had to

go to bed almost as soon as I had taken a hasty meal Sometimes the exhaustion was such that despite the need of sleep and a drowsiness which prevented me even from reading the papers, I could go to sleep only after many hours

Today and since the second day, and above all the third day after the first injection, all that has changed and I have regained at least all the force which I possessed a number of years ago Experimental work at the laboratory tires me little now I can, to the great astonishment of my assistant, remain standing for hours together without feeling the need of sitting down There are some days when after three and a quarter hours of work standing, I have been able, contrary to my habits for twenty years, to work at the preparation of a memoir for more than an hour and a half after dinner All my friends know what an immense change that implies for me [24]

I can also now without difficulty, and even without thinking about it, go up and down stairs almost running, a thing which I always did before the age of sixty [25] By using the dynamometer, I have established that there has been an incontestable increase in the force of my limbs For my forearm, in particular, I find that the average of trials since the first two injections is greater by 6 7 kilograms than the average before the injections

His early attempts to measure "nervous force" had led Brown-Séquard to keep a record of the strength of the flexor muscles of his arm, which he

measured by means of a dynamometer The actual figures which he gave in a later paper were in 1860, 50 kg , 1863, 46 kg , 1889 (up to May 15), 27 kg , May 16, 1889, 41 kg We may be spared the intimate details of the measurements of the increase in the distance he could propel a jet of urine, or the astonishing return of natural ease in defecation without need of recourse to purgatives He thought that both his physical forces and his mental faculties had benefited enormously from the injections He was perfectly aware of the possibilities of auto-suggestion, but he was convinced that the improvement was real, not imaginary From this moment until his death, four years later, rejuvenation filled his every thought The entire course of events may be followed in detail in the exchange of letters between d'Arsonval and himself

At first glance it would appear that he overdid the treatment and carried rejuvenation too far, since it is an established fact that by autumn he was suffering from whooping cough At Nice, however, he began to recover from this untimely malady, and was able to devote considerable time to his *Archives* Although he was now the sole editor of this journal, he proposed to acknowledge the help of his friends by

placing on the cover of the issues in 1890 the names of Dastre, Franck (1849–1921) and d'Arsonval. His letter of December 6 to d'Arsonval reads:

> You see I have regained my vigor. Since yesterday all my troubles have completely disappeared, I sleep and I eat as I did last July and August. My wife is also well. Charlotte[36] did not catch the whooping cough.[37]

But, unhappily, a fortnight later he was still whooping three to four times daily.

From the moment of his announcement of the effects of his extracts on himself the medical world was in a furor. His tremendous reputation, recognized all over the civilized world, was a guarantee of good faith, and the wonder-working extract was tried out for almost every debility known to man. From outposts like Bucharest and St. Petersburg enthusiastic reports began to come in, the extract hastened transmission of sensory impulses, an overwhelming number of locomotor ataxia victims were helped, there was immunization against tuberculosis, augmentation in the vigor of the foetus of a syphilitic mother, and twenty-one cases of cancer had been ameliorated. Before the end of the year more than twelve thousand physicians were administering the extract to their patients.

The public press played the matter up in a most sensational manner, but medical journals were, on the whole, hostile In America Brown-Séquard was accused of thinking he had discovered "a sort of vital elixir or fountain of perpetual youth", the British thought "injection of seminal fluid of dogs and rabbits into man disgusting" Expressions such as "elixir of youth," "The Alchemist's Dream," "senile folly," "shameful discredit to the profession," were bandied about One American physician, writing in a magazine, *The Open Court*, said, "The idea is as old as stupidity, wicked as superstition, cruel as savagery, it is false in its premises, false in its logic, false in its conclusions" A French critic said that the idea was to be found in a pharmaceutical concoction of 1540, and concluded his article eruditely with the Latin tag, "Nil sub sole novum!"

Ridicule is no deterrent to the zealous, and Brown-Séquard, together with his laboratory staff, d'Arsonval and Hénocque, thoroughly believed in their testicular extract Because the subcutaneous injections were troublesome, Brown-Séquard began to use intrarectal applications in 1890 and thought the results satisfactory, although a stronger solution was necessary to bring about the desired results than

when administered subcutaneously Throughout all the turmoil they tried to maintain a thoroughly scientific attitude When one Parisian physician wished to publish an account of a patient cured of pulmonary tuberculosis by the extract, Brown-Séquard made him wait until he had at least three cases to report Although he gave credence to cures of 'galloping consumption," he wrote to d'Arsonval

For you and me, there is a very simple explanation of these remarkable facts, the cure depends on this, that as the nervous centers gain in force, the patients produce less pulmonary poison

The testicular extract was not, in Brown-Séquard's opinion, a specific cure for every known disease, his scientific experience told him that such an idea was absurd, what he thought it did was to build up the vigor (or, in his own phrase, the "nervous force") of the patient, so that he could better overcome any disease which attacked him, whatever its nature Just as all his own bodily forces had been raised above their previously diminishing level to something approaching their former vigor, so the efficacy of the extract lay in its building up the strength and resistance of the patient The cult of injection spread like wildfire

In November Brown-Séquard learned of the success of the great German bacteriologist, Robert Koch (1843-1910), in extracting from the tubercle bacillus a substance which deterred the growth of other cultures of the bacillus The product, tuberculin, was hailed as a specific cure for tuberculosis and every tubercular patient who could obtain injections was thought to be on the highway to recovery from the disease The two years after Koch announced his discovery have been described as the era of "Tuberculin Delirium"—a decade of "Tuberculin Execration" was to follow[1]

Brown-Séquard's immediate interest in Koch's discovery was to relate it to his general theory of the mode of operation of his own extract He wrote to d'Arsonval

You will learn with the greatest satisfaction—if you do not know it already—that the cure of tuberculosis by the substance injected by Koch takes place *without the bacilli being killed* These '*Don Quixote Windmills*,' these innocent bacilli, do not die until after some time, that is to say when the substrate which is favorable to them has been altered and had ceased to exist That is how M Koch gives us the victory! We shall not delay in thanking him

Prepare to go ahead and do the experiments of which I spoke to you as soon as you have obtained a sufficient

quantity of Koch's liquid You must go to see M Liard and M Yves Guyot [38] and get them interested in obtaining for you through the French ambassador in Berlin a sufficiently large quantity of Koch's liquid, *as soon as it can be procured*

Don't go to sleep on the job

I am better as you see and I am on the alert Send me the news

Heartily yours [39]

At the very end of the year, 1890, Brown-Séquard wrote to d'Arsonval that he had become extremely weak again His dynamometer registered only 28 instead of 42 He thought he would have to return to subcutaneous injections, but he had no filter at Nice to prepare the extract If d'Arsonval could find a suitable piece of apparatus, would he send it immediately by express? He had also decided to add some salicylic acid to the extract

All the Parisian physicians were demanding the extract and expected to find, as Brown-Séquard said, "a Fountain at our laboratory," but his answer to them was that d'Arsonval and Hénocque could not spend any more time than they were already giving in its preparation For some time now the extract had been given to physicians without charge and its

sale was forbidden Directions for its use had been printed and the leaflet bore the stamp "Laboratoire de Médecine du Collège de France," and the names of both Brown-Séquard and d'Arsonval appeared at the bottom Soon legal complications developed In the *Société de Biologie* Brown-Séquard accused charlatans of making testicular extracts and selling them under the name of "Elixir" He tried to have these persons legally restrained from making the extract, even though they prepared it according to the directions which he had published in the scientific journals A lawyer on consultation informed him that there could be no restraint, since a scientific communication, once published in the journals, no longer belonged exclusively to the author, but was everybody's possession

In the middle of February, 1891, Brown-Séquard learned that Professor Poehl of St Petersburg had prepared a salt of spermine, and he was anxious to compare the effects of a solution of it with d'Arsonval's preparation [40] This is the earliest reference in Brown-Séquard's correspondence to a preparation which was put on the market and thus became the first endocrine product to be commercialized Its sale was so widespread that it soon reached even the out-

posts of the British Empire, and a doctor in South Africa is reported to have laid down in his cellar barrels of the stuff which were never opened George W Corner [41] makes Brown Séquard's "notoriety" "responsible for exploitation of endocrine preparations in the drug trade ahead of scientific knowledge" It is perfectly true that there was inadequate control in all this work, but the staff at the *Collège de France* was so convinced of the beneficial effects upon the elderly professor in spite of his bouts of illness, and they were so influenced by the reports of thousands of reputable physicians having used the extract with notable success that they felt justified in making their discovery immediately available in medical treatment

The ball had been started rolling by Brown-Séquard and had been given a violent push by Koch, so that physicians began to demand, for injection into their patients, preparations of spinal cord, liver, kidney, thymus and other organs [42] Brown-Séquard therefore began experiments in Nice on guinea pigs, injecting them with extracts of various bodily organs All animals so injected died, except the one receiving extract from the suprarenal capsules This result led him to telegraph d'Arsonval in Paris not to waste

animals on the project Nevertheless, he did not abandon the idea, for in March he wrote that his assistant might try out his special filter on extracts of "liver, spleen, kidney, suprarenal capsules, pancreas, thyroid, lungs, salivary glands, brain and cord" That he was on the right track is shown by the following letter

I say now merely that all glands with an external secretion have at the same time, like the testicles, an internal secretion The kidneys, the salivary glands, the pancreas are not merely organs of elimination They are like the thyroid, the spleen, etc, organs giving to the blood important principles, either in a direct manner, or by resorption after their external secretion Uremia, jaundice, like tetany after removal of the thyroid, depend in part on the absence in the blood of certain principles, which an injection of renal or hepatic fluid could cause to disappear [43]

This is indeed a prophetic statement in the light of recent physiological discovery

Brown-Séquard was interested to learn whether the internal secretion might also be found contained in the external secretion, and whether it might perhaps be resorbed into the blood This was brought out in his suggestion for experiments to be performed by d'Arsonval on the pancreas He wrote

When the pancreas has been *suppressed* (ablation, ligature of its vessels, etc.) there is diabetes. Would there be no diabetes if, after suppression of the functions of the gland, there were injected an extract of this gland taken from a healthy dog? [illegible] Would the secretion of this gland taken from the pancreatic duct prevent diabetes from appearing after suppression of the gland, as well as an extract [illegible] the gland?"

This was an excellent program for research and d'Arsonval tried out [illegible] experiments. Unfortunately, he met with the same difficulty which held up the preparation of [illegible] for another thirty years, namely, the separation [illegible] the digestive qualities from the gland. The presence of such qualities determined [illegible] deleterious properties which the extract [illegible].

All these studies on organic tissue extracts were incorporated into papers for the *Société de Biologie*, which bear the names of both Brown-Séquard and d'Arsonval. In [illegible] dated April 18, 1891, by the latter in the presence of the professor, who was still at New Haven, occurred the memorable statement:

[illegible] glandular organs, [illegible] to the blood [illegible] internal secretion. We [illegible] that all tissues can and should be

employed in special cases as a mode of treatment, that, in a word, there must be created a new system of therapeutics, the medicaments of which will be products made from the different tissues of the organism The field opened to research along this path is immense

This clear statement is the very basis of modern organo-therapy, and in spite of the blind alley into which their own experiments had led them, the world owes a great debt to these two investigators for pointing out the way to obtain some of the most effective therapeutic agents in our possession, the possibilities of which are being intensively explored at the present time

At the same session of the *Société de Biologie* at which the creed of the endocrinologist was announced, Gley reported that as yet he too had not succeeded in obtaining an extract of pancreatic tissue which would ameliorate the glycosuria of depancratized animals, because, like d'Arsonval, he had not been able to eliminate the toxic effects of the pancreatic ferments, but he had succeeded in stopping convulsions in thyroidectomized animals by injections of an extract of thyroid tissue That the parathyroids are distinct from the thyroids in which they are imbedded had not yet been definitely

established This paper was one of several written by Gley in this year which finally settled this point At its close he generously added these words

The importance of these new data will undoubtedly be appreciated from the point of view of the general physiology of glands, data which seem to confirm certain ideas put forth by M Brown Sequard regarding such physiology

The enigmatic endocrines had begun to assume their rightful place in physiology thanks to Brown Séquard

Brown Séquard's health, which at first had been the index of the efficacy of the testicular extract, had broken down at the end of 1890, and early in 1891 he nearly died During all this the injections were continued The matters of the strength of the extract and the best type of preservative were earnestly debated by letter with d'Arsonval, for the injections did in fact cause very bad reactions, including persistent indurations of the abdomen and hips as large as cherry pits Brown Séquard was attacked by a severe rheumatism, and even after the worst of his illness was over, phlebitis in one of his legs kept him, as he wrote, "nailed to the bed or the sofa" It was only in May of 1891 that he was sufficiently recovered to return to his apartment at 19, rue François Ier in Paris He visited the laboratory and

urged on the research D'Arsonval escaped to his place near Limousin from July until November in the pursuit of his own affairs, but he apologized for not being at the professor's disposal in Paris, and wrote long answers to miscellaneous questions It was in October of this year, just before Brown-Séquard set out for another winter in Nice, that Condé-Williams, Judge of the Supreme Court of Mauritius, came to call on him and contributed this word picture of his host

> I found him a gentle, modest, white-haired old man, rather below the middle height, of manners quiet and unassuming and a smile full of kindness [47]

To this portrait may be added his daughter's recollection that her father was always particularly neat in his dress and careful of the appearance of the black frock coat which he always wore

The extract appeared to be efficacious once more, for on the eve of the departure for Nice, Brown-Séquard was able to remain on his feet for sixteen hours supervising the packing of his books, manuscripts and instruments When he arrived the next day at his winter quarters, having had little sleep on the train, he showed no signs of fatigue—all this

at an age of seventy four years and eight months, as he was proud to point out in his account to d'Arsonval The family was reinstated in *Villa Mon Plaisir*, Avenue St Lambert, and the laboratory was set up in the adjoining coach house as usual

In April 1892, Hédon performed his classic experiment on grafting pancreatic tissue beneath the skin of a dog, then removing first the dog's own pancreas and finding no trace of glycosuria, and finally removing the graft and finding intense glycosuria Brown Séquard wrote the details of this experiment with exclamation marks to d'Arsonval in the same letter in which he informed him that the broken point of a needle lodged in his side was giving him trouble

In Paris the turmoil over the testicular extract continued For two years d'Arsonval had been fighting a delaying action at the laboratory against mounting requests for his product, but the time had now come when the laboratory of the *Collège de France* could no longer undertake to supply the demand In July, 1892, a bulletin had to be sent out to the effect that the extract would be sent only to persons whose treatment had already begun and to physicians who needed it themselves Up to this

time Brown-Séquard had given the extract to physicians without charge He had personally paid all the expenses, which amounted eventually to a sum of about 10,000 francs He would permit no one except d'Arsonval to make the preparations, so that he might be sure that they were made correctly and were free from microbes Commercial companies fought for a chance to manufacture the extract at a profit with the authorization of the laboratory, but both investigators refused to consider this The unauthorized use of Brown-Séquard's name in pamphlets and on labels could be, and was, made a ground for legal proceedings The German government had taken charge in the case of Koch's tuberculosis preparation, "Kochine," and there were demands in the French newspapers that their state take on the preparation of what was now known as "L'Extrait-Brown-Séquardien" D'Arsonval was informed by the authorities that the French government was unwilling to take this step, and he was advised "to publish *in extenso* the full procedure for making the liquid with all the precautions to be taken" In reality, the preparation of the extract was not difficult The directions followed in 1892 by Dr Constantin Paul, with the approval of Brown-

Séquard were as follows "A male guinea pig was killed by a blow; the testicles were removed, macerated for 24 hours in three times their weight of water at 25°, the glycerine having previously been heated to 140°; the glands were then minced with scissors, distilled water was added, and the emulsion was filtered; the resulting liquid was sterilized by carbonic acid under pressure."

In spite of all Health his incessant experiments, and the loss of fur over the extinct, Brown-Séquard found time to come up to Paris to give a public lecture on July 1 at the Hotel Continental, the proceeds of which went to aid victims of a violent cyclone which had devastated Mauritius on April 29, and had caused much damage. He wrote to Mauritius

I was deeply moved at the news of your cyclone. I have done what I could to come to the aid of the victims [illegible]. I have since found the means to remain poor, and I can give only a very small sum, but I have given what I could at the price of pains. My lecture produced quite a large sum. It could have done better at any other time, Paris was empty.

One of his letters in this year shows that Mme Ramdohr, who had been the friend of Claude Bernard in his last years, had maintained her con-

tacts with the incumbents of the Chair of Medicine at the *Collège de France* She had entertained Brown-Séquard in Paris just before his departure for Nice in November, 1892, and when the family was established on the Riviera, they returned the invitation while Mme Raffalovich and her husband were in Nice at the end of the month

Shortly after this Brown-Séquard tried to obtain a regular appointment for d'Arsonval through the creation of a Chair of Biological Physics, but Renan, President of the *Collège de France*, thought the case hopeless, since the Chamber of Deputies was feeling particularly economical at this time However, Brown-Séquard made up a list of all the influential persons d'Arsonval was to call upon, and we find that Mme Raffalovich was still a power in high places "Mme Raffalovich must win over the Minister, M Bourgeois, to your side," he wrote Out of a list of nine obligatory names, hers was fourth in importance Unfortunately, the plan did not succeed A proposal was made that the Chair of Chinese be turned into a Chair of Biological Physics, but Brown-Séquard had to inform d'Arsonval, "You have a competitor, a M de Rosny, a Chinese,"—the scheme had fallen through However, when d'Arson-

val was about to give the professor's winter lectures for him according to the established custom, Brown-Séquard advised him, "Open the course with lectures on Biological Physics, what it is and what it can be." Although the Chair had the title of Experimental Medicine," Magendie and Bernard had both been very liberal in their interpretation of the field covered, so there was a good precedent for d'Arsonval to branch out in the direction of his specialty.

Members of the medical profession still clamored for more and more testicular extract. In September, 1892, Brown Séquard and d'Arsonval had limited to 1200 the number of physicians to whom they furnished it. They wished to restrict distribution to those who would provide case histories of the patients who received injections. Brown-Séquard urged the profession to demand that the government "take on the preparation at the Central Pharmacy to sell at cost price to all the physicians in France who want it. As to making our laboratory a sort of Pasteur Institute, we cannot do that." At the end of the year d'Arsonval had difficulty in getting from slaughter-houses material for his own preparations, since Charcot, who at first had been recalcitrant, was now draining their resources to make extract for use

at the huge neurological hospital, the *Salpétrière* Brown-Séquard, on learning of this, remarked suspiciously that Charcot would probably only try to prove that the extract was valueless [40] By June of 1893 the demands had reached such proportions that the laboratory at the *Collège de France* could only in fairness stop free distribution altogether

Brown-Séquard was well enough to give the spring course of lectures for 1893 in person, and in that year he also made his last report to the Academy of Sciences He presented the following list of cures claimed for the testicular extract the best results were obtained on locomotor ataxia, 314 out of 405 patients having been benefited, and even Friedrich's hereditary locomotor ataxia was helped, sclerosis of the cord showed 80-90% of cures, for pulmonary tuberculosis there were four cures in every five cases, night sweats, coughs, feebleness, digestive troubles, insomnia and fever were stopped, cancer was benefited, cases of heart disease, brain trouble, kidney disease and myelitis were helped, paralysis agitans, said to be incurable, yielded astonishing results, diabetes was alleviated, arteriosclerosis of almost every organ of the body, goitre, debility of old age, hysteria, chorea, headaches, gout, neurasthenia yield-

ed to treatment, to the author's surprise, wounds healed faster in guinea pigs when bathed in the fluid. In short, there was hardly an ill to which the flesh is heir at all out which there had not been a report of some amelioration after injection of testicular extract. Again Brown Séquard was careful to state that the beneficent effects were not the result of a curative influence on the morbid state itself, but the nervous system so gained force that it was able to cope with the disease, or perhaps the blood was helped to form new elements which were curative. Although this was his first appearance before the Academy of Sciences,[3] he continued to describe before the *Société de Biologie* his animal experiments on injection of extract of the suprarenal capsules, thyroid, spleen, bone marrow. A combination of the last three extracts he recommended to physicians in the treatment of acromegaly. Although he considered it not strictly necessary, he advised that the injections of extracts of spleen, thyroid and bone marrow be accompanied by daily injections of the testicular extract, which now went under the name "le liquide orchitique."[51]

Brown-Séquard, suffering himself with phlebitis in his leg, was also worried about his wife's health

They left Paris in July, 1893, for Sainte Adresse (near Le Havre), and he had to write to d'Arsonval to send some garden chairs, his box of instruments, a bundle of library shelves and four crates of guinea pigs The rheumatism was very bad and the injections very painful, but he continued to work He reported, however, that his wife was doing well in their retreat The return to Paris in September did not contribute to their comfort When November saw them again at *Mon Plaisir* in Nice, the injections were credited with making Brown-Séquard able to stand not only the journey but four nights without sleep (partly on account of the mosquitoes) without fatigue The guinea pigs also arrived in Nice " alive and doing well," all except those with amputated legs, which he was observing for transmission of acquired characters

In February, 1894, while he was confined to his bed with his phlebitis, Mme Brown-Séquard died The bereaved husband was inconsolable He refused to eat, could not sleep, and rapidly began to decline himself He said, " I can't work any more It is all over " Aggravating legal difficulties in settling his wife's estate were only reminders of his loss Although it was still winter he could not bear to

remain in Nice He felt he must get away, if only to Paris D'Arsonval wrote urging him not to attempt the journey, and especially warned him to "let the phlebitis calm down a little Movement is so dangerous with clots in the veins" But he would not heed the advice Early in March he was reestablished in the rue François Ier On the 23rd he wrote to d'Arsonval that only his phlebitis prevented him from leaving for England to discuss the settlement of his wife's estate with her relatives On the 24th he was suddenly taken with vertigo, his sight was affected, and he became unconscious When he recovered consciousness, his speech was thick and embarrassed He exclaimed, "This is an attack of epilepsy"

Dr Eugene Dupuy was in attendance and tried to persuade the invalid to remain in bed He insisted, however, on sitting up to write letters It had been his custom for the last two years to carry on a voluminous correspondence, running to as many as eighty letters in a single day The letter which he wrote three days later, on Tuesday, to his old friend and his wife's cousin, Dr W D Waterhouse, who was also one of the London physicians to whom he had been supplying testicular extract, was later

published in the *Lancet* and gives the details of his seizure

My leg being much worse, I have had to give up the hope of going to England But the bad state of my leg (swelling and pain) is nothing in comparison with the very grave cerebral symptoms that have come since In the first place my sight has become almost suddenly very poor—this is persistent, and another slight trouble, almost constant, but not absolutely so, exists, it is a complete loss of the sight in a small part of the vision field constituting hemiopia, limited to a small part of the left of the two retinae This is, of course, of cerebral origin, but it does not seem to be of organic origin because it is not absolutely constant Most likely there is either inhibition or a vascular spasm which destroys at times the power of sight in two small parts of the retinae This began on Sunday The next morning something worse occurred My life, and all that occurred for many months lately, became suddenly a blank I found that I was in my small library, but although recognizing the room and the various objects in it, I did not know where to locate that room, at Nice, in Paris, or in some other place This lack of memory of everything lasted at least 2 or 3 hours I knew I was mentally suffering in some way, but nobody found that there was something wrong about me except a faithful servant who had been with us since 1876, to whom I said I was not well and might suddenly be struck with loss of consciousness (apoplexy), paralysis or convulsions, and I

advised her what to do if anything very bad occurred . Yesterday I had a good many visitors (when they came the attack was over), and I talked rationally with them, saying but little of what had occurred Today I have perhaps less of the hemiopia, but the dulness of sight is at times as great as yesterday No other symptom, no paralysis, no rigidity, no numbness, no alteration of the power of speech, no titubation There may have been a very small focus of softening or haemorrhage, but the principle direct cause of the symptoms must have been a vascular trouble or some purely inhibitory effect due to the constant irritation of the brain or to some gastric or bowel trouble [32]

The last sentence shows how firmly fixed in his mind were his theories of " inhibition " and " action at a distance " These themes, which had been sounded for years, now reappeared in the *finale*, like motifs in a well-constructed musical composition

On Friday he seemed somewhat improved He took some nourishment and seemed cheerful, but at the end of the day Dr Dupuy noted that the patient's face was flushed, and the vertigo and hemiopia distressing Brown-Séquard had insisted on crawling from room to room on all fours, all the while giving an analysis of his case and a prognosis, as if he were dealing not with himself but with another patient The following day he was unable to speak, the

right side of his face was paralysed and his left arm as well Saturday he tried to write on a slate, but the only recognizable word was "hyperaesthesia" However, he gave evidences of pleasure on seeing his friends On Sunday, April 1st, at 2 a m, he lapsed into unconsciousness, lingered on throughout the day and died near midnight There was no post mortem, but it was evident that his own diagnosis of softening or hemorrhage on the right side of the brain was correct It shows unusual mental vigor for him to have been able to write so clear an account of his state to his friend, Dr Waterhouse, several days after the trouble had actually started

On Monday when the Academy of Sciences met the president announced the death of their *confrère*, and the session was immediately adjourned in his honor The International Congress of Medicine was at this moment being held in Rome, and when a telegram announcing the death of the famous scientist was read before the section of Physiology, it was voted to send a telegram of regret to the president of the Academy of Sciences After a simple funeral ceremony (he was not of the Catholic faith, but a Protestant) Charles-Édouard Brown-Séquard was buried in the cemetery of Montparnasse, and on

his coffin was placed a wreath in token of esteem from far away Mauritius.

5

Brown Séquard was the last in the line of a great tradition of French experimental physiology at the *Collège de France*, for d'Arsonval, who succeeded him in the Chair there, achieved his fame in the field of electricity Magendie, Bernard and Brown-Séquard spanned the XIX century from its first decade to its last, and from their work came the ideas whose fulfillment now occupies much of our present day investigation Magendie had the greatness of the pioneer It was his independence and originality of mind which broke away from the old tradition Claude Bernard possessed in most perfect balance imaginative and critical powers His intuitive approach, which made possible his beautifully planned experiments, was matched by his painstaking integrity in executing them Brown-Séquard's intuitive powers were as remarkable, if less controlled, than those of Bernard An anonymous contemporary said that he "worked by intuition, his induction being singularly rapid, apparently savoring

of revelation" He was very quick to grasp the implications of the work of others, and this served him well in his experiments on vasomotor nerves and the adrenals His weaknesses, more apparent in his later than in his earlier work, were his lack of capacity for self-criticism and his tendency to exaggerate the scope of a few favorite theories His earliest discovery, the crossing over of sensory impulses in the spinal cord, is classical in method and a completed study His work on epilepsy, and the related experiments on heredity, which absorbed so much of his time and energy, on the contrary present a distressing picture of blindness to inconvenient facts, and the uncritical interpretation of data in terms of a favorite hypothesis, action at a distance His continued and fanatical devotion to this idea even led him into an unlucky opposition to the fruitful doctrine of cerebral localization At the end of his career, his broad general conception of the possibilities of organotherapy seems to arise from an almost prophetic instinct, but his experimental evidence carries no conviction to us today Even his basic finding, upon which the whole vast structure rested, death after removal of the adrenals, is called in question when we consider that the brief time of

survival which he reported is more indicative of death from shock than from a well conducted adrenalectomy His drive, his fever of work, a quality so fundamental for an experimenter, equalled, if it did not surpass, the measure of the trait in Magendie and Bernard, but he did not submit to the strict discipline of the laboratory continuously enough to fulfill the promise shown by his accomplishments before 1856 The opportunities of holding an academic post which were offered him in middle life did not really attract him, because, after all, he found teaching as much of a distraction from investigation as medical practice He did not gather a group of devoted pupils at the *Collège de France*, comparable to the one which surrounded Claude Bernard at the end of his life, but he was content to have Dupuy, d'Arsonval and, later, Hénocque on call to carry out his instructions His neurological practice was, in fact, the mainstay of his career, for it secured him not only his livelihood and an international prestige, but was also the focal point of much of his research He left an indelible mark on physiology and medicine, and we look back on him as a brilliant and indefatigable investigator and a

courageous human being, who, when he thought that he himself could best serve as the subject of an experiment, did not hesitate to submit even his own body to the test

NOTES

CHAPTER III

[1] [illegible], *[illegible] Clinic [illegible]*, Bal[illegible] [illegible], 19[illegible]

[2] [illegible] 2 2 [illegible] [illegible] of the quarrel, [illegible] [illegible] [illegible] [illegible]

[3] *C. R. Soc. [illegible]*, [illegible]

[4] *Ibid.*, [illegible], *C. R. Acad. d. Sc.* [illegible]

[5] *C. R. Acad. d. Sc.*, [illegible], 1[illegible]

[6] *Ibid.* [illegible]

[7] *Ibid.*, 52 1317, [illegible]

[8] [illegible] *Text[illegible]* [illegible], Edinburgh and [illegible], 19[illegible], vol. 2, p. 137

[9] [illegible] vol. 2, p. [illegible]

[10] *[illegible] de Méd.*, [illegible] 2, 1[illegible]3

[11] *C. R. Soc. de Biol.*, 2 10[illegible], 1[illegible]0

[12] *Ibid.*, 2 1[illegible]9, 1[illegible]3

[13] *L[illegible] Med. & Surg. J[illegible]*, 55 [illegible]3, 18[illegible]6

[14] [illegible] are now [illegible] it [illegible] be useful to refresh the [illegible] a moxa is a soft woolly [illegible] prepared from the [illegible] leaves of a Chinese worm wood, and used as a cautery by burning it on the skin; by extension, any [illegible] used in like manner as a counterirritant is termed a moxa

[15] *C. R. Acad. d. Sc.*, 42 [illegible], 1856

[16] *C. R. Soc. de Biol.*, 11 191, 1859

[17] *Proc. Roy. Soc. Lond.*, 10 297, 1860

[18] *C. R. Soc. de Biol.*, 21 111, 1869

[19] *Ibid*, 22 5, 1870

[20] Delhoume, *op cit*, p 348

[21] *C R. Soc de Biol*, 22 64, 1870

[22] *C R. Acad d Sc*, 94 697, 1882

[23] *Ibid*, 115 394, 1892

[24] *C R. Soc de Biol*, 116 314, 1934 and 119 692, 1935 *Presse méd*, 44 1889, 1936

[25] *C R Acad d Sc*, 94 491, 1882 Cf Aub, J C, *Journ Indust Hyg & Toxicol*, 26 183, 1944

[26] *C R. Acad d Sc*, 94 1285, 1882

[27] *Ibid*, 95 553, 1882

[28] Delhoume, *op cit*, p 264 There is no evidence that Brown-Séquard shared his assistant s low opinion of du Bois-Reymond In his earlier days Brown-Séquard was only too eager to have the German professor learn of his own work, since (preserved in the John Crerar Library in Chicago) there is a copy of his lectures published in 1855, inscribed in faded brown ink, 'Dr Dubois-Reymond, Berlin, with the best regards of the author ' Then follows a squiggle which might be interpreted as "EBS '

[29] *Révue Scient*, 4e sér, 1 473, 1894

[30] A portrait representing a fairly young man with a black beard which often appears as an illustration of biographical sketches is denied by his daughter to be really a picture of her father, although some authorities who knew him in Virginia in the 1850 s have affirmed that it is a good likeness There is, besides the Emperor's photograph, which has been widely reproduced, a lithograph by Gillet, taken from a painting by a Mauritian painter, Sérendat de Belzim, which Mrs McCausland also thinks has no resemblance to her father, and a bronze bust by the sculptor, C. de Swiecinski, erected with appropriate ceremony in the Jardin de la Compagnie in Port Louis in 1928 to replace an earlier one of imitation marble broken by being hurled to the ground in a hurricane

[31] *C R. Acad d Sc*, 105 1056, 1887, 106 106, 1888

[32] Delhoume, *op cit*, p 341

[33] Delhoume, *op cit*, p 261

DUNBAR, N *The "Elixir of Life"* J C Cupples Co, Boston, 1889 110 pp

DUPUY, E Notice sur M le professeur Brown Séquard, ancien Président de la Société de Biologie *Mém de la Soc Biol Paris*, 46 759 770, 1894 *V* also *Révue scient*, 4e sér, 2 737-743, 1894

FRANCIS, S W Biographical sketches of distinguished New York physicians C E Brown Séquard, M D, F R S, etc *Med & Surg Reporter, Philadelphia*, 15 169-172, 1886

GLEY, E C-E Brown Séquard *Arch d Physiol norm et path*, 5e série, 6 501-516, 1894, *Biol centralbl*, 14 785 800, 1894

KELLY, H A and BURRAGE, W L *American Medical Biographies* The Norman Remington Co, 1920, pp 155-157

MAJOR, R H Charles Edward Brown Séquard *Essays in Biology in honor of Herbert M Evans* Univ of Calif Press, Berkeley and Los Angeles, 1943, pp 369-377

OGLE, J W Further remarks on Dr Brown Séquard s last illness *Lancet*, June 2, 1894, p 1391

OTT, I Dr Brown Séquard *Med Bull Philadelphia*, 18 361-366, 1896

POWER, d A *Dict Nat Biog* 1917, vol 22 suppl, pp 319-321

PUTNAM, T J Charles Edouard Brown-Séquard *Proc Amer Acad Arts and Sci*, 30 589 592, 1894-95

RICHET, C Brown Séquard *Dict de Physiol*, Felix Alcan, Paris, 1897, vol 2, pp 256-261

ROUGET, F A *Brown Séquard et son œuvre Esquisse biographique* The General Printing and Stationary Cy Ltd, Port Louis, Ile Maurice, 1930 160 pp *Renseignements supplémentaires*, 21 pp

TUCKER, B R Charles Edouard Brown Séquard (Pamphlet enlarged from article published in the *Bulletin of the Richmond Academy of Medicine*, June, 1937)

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